THE PATHOLOGY OF THE EYE

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PATHOLOGY OF THE EYE

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VOLUME I

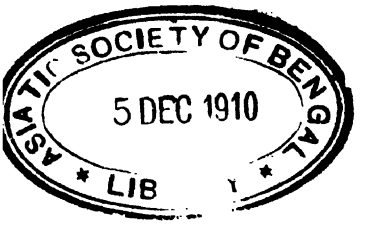
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PREFATORY NOTE

NO complete monograph on the Pathology of the Eye has yet been written in any language. Various attempts have been made from time to time to describe and illustrate the chief facts of the pathological histology by Wedl (1860), O. Becker (1874), Pagenstecher & Genth (1878), Alt (1880), Wedl & Bock (1886), Greeff (1902), Ginsberg (1903), and others. All of these, with the exception of Ginsberg's Manual and the incomplete work of Greeff, are inadequate and out of date; and even the latter works are not available for all English-speaking ophthalmologists.

The object of this treatise is to give as complete an account of the Pathology of the Eye as is possible in the present state of our knowledge. It may be reasonably asserted that the time is not ripe for such a work, and as far as dogmatic finality is concerned this is true. There are few, however, who will not admit the urgent need of gathering together the grains of knowledge which we possess, and winnowing them of the chaff of futile conjecture and discredited theory.

It must be admitted with regret that few of the problems before us have been solved. I shall therefore endeavour to set forth the facts which have been discovered, and which have been recorded in the various European and American scientific journals. The various theories based upon these facts will be reviewed and weighed, with the object of determining their relative value, and of arriving at the best working hypotheses for directing future research.

It is not to be expected that my deductions will meet with unqualified approval. I shall be satisfied if the facts, and the theories

founded upon them, are accurately reproduced, so that future workers may find a safe foundation prepared upon which to build.

The work will be divided into four volumes, the first two dealing with the Pathological Histology of the Eye, the last two with the General Pathology of the Eye.

In Volumes I and II the parts of the eye and its annexes will be taken *seriatim*, and the histology of the various morbid conditions described.

In Volumes III and IV the diseases which affect the eye as a whole will be discussed, and an endeavour will be made to trace them to their ultimate causes. They will therefore include such conditions as glaucoma, sympathetic ophthalmia, congenital malformations, etc. The microscopic features of these conditions will be more conveniently dealt with in immediate relationship with them.

PREFACE TO VOLUME I

THIS volume includes the Pathological Histology of the Lids, Conjunctiva, Cornea, Sclerotic, Iris and Anterior Chamber, and Ciliary Body, together with the Bacteriology of the Conjunctiva. The Normal Histology of the parts is briefly related, no attempt being made to give an exhaustive description. Only those features which have a special bearing upon pathology are more fully dealt with; these are often inadequately discussed in the ordinary text-books of normal histology.

All the new illustrations are from photographs, which have not been touched up in any way. I am of the opinion that for elementary teaching good drawings are superior to photographic reproductions, much detail being obscured in reproduction by half-tone blocks. In an advanced work of this kind, however, a good knowledge of normal and general pathological histology is taken for granted, and absolute fidelity is of prime importance. It is above all things essential that the text-book shall subserve, and not replace, work in the laboratory.

I am greatly indebted to the recent books of Greeff and Ginsberg in preparing this volume. I have made a point, however, of going to original sources for information; but the arduous task of discovering references has been much facilitated by these works.

I am also under a deep obligation to the Staff of the Royal London (Moorfields) Ophthalmic Hospital: without their assistance the work could never have been attempted. I have had every opportunity of utilising the valuable pathological material which

has come immediately under my notice as Pathologist, as well as that which has accumulated under the supervision of my predecessors.

I am further indebted to the Ophthalmological Society of the United Kingdom for permission to reproduce illustrations from their 'Transactions.'

Professor Fuchs has kindly sent me from time to time specimens from his valuable collection. Some of these I have photographed and reproduced.

All the material which I have borrowed from others has been acknowledged in the text; any omissions in this respect have been unintentional. For the remainder I am alone responsible.

Mr. W. I. Hancock, F.R.C.S., has kindly assisted me in revising the proof sheets.

J. HERBERT PARSONS.

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ABBREVIATIONS

A. d'O.—Archives d'Ophthalmologie.

A. f. A.—Knapp and Schweigger's Archiv für Augenheilkunde. (Articles in A. f. A. are often translated or abstracted in A. of O., and *vice versâ*; the reference is usually given to one only.)

A. f. O.—v. Graefe's Archiv für Ophthalmologie.

A. of O.—Knapp's Archives of Ophthalmology.

B. d. o. G.—Bericht der ophthalmologische Gesellschaft zu Heidelberg. (The earlier reports are contained in K. M. f. A.)

B. z. A.—Deutschmann's Beiträge zur Augenheilkunde. (The reference is given to the part [Heft], not to the volume.)

C. f. A.—Hirschberg's Centrablatt für praktische Augenheilkunde.

G.-S.—Graefe-Saemisch, Handbuch der gesamten Augenheilkunde. (The date determines the edition: 1st edition, 1874—1877; 2nd edition, 1898— .)

K. M. f. A.—Zehender's Klinische Monatsblätter für Augenheilkunde.

R. L. O. H. Rep.—Royal London Ophthalmic Hospital Reports.

T. Am. O. S.—Transactions of the American Ophthalmological Society.

T. O. S.—Transactions of the Ophthalmological Society of the United Kingdom.

Z. f. A.—Zeitschrift für Augenheilkunde.

*.—The most important articles are marked with an asterisk (*).

CHAPTER I

THE LIDS

THE NORMAL LIDS

THE lids are covered anteriorly by skin and posteriorly by mucous membrane (conjunctiva tarsi); they end in a free edge (margo intermarginalis) about 3 mm. broad. The substance of the lids consists of muscles, glands, blood-vessels, and nerves, all bound together by connective tissue, which is particularly dense at the posterior part, where it forms a stiff plate, the tarsus.

The skin of the lids differs from that of the rest of the body merely in its thinness, its loose attachment, and the absence of fat in its corium; the papillæ, too, are less marked than in other parts. It is covered with fine downy hairs, which are provided with small sebaceous glands, and there are also small sweat-glands. The stratum Malpighii of the epidermis often contains pigment, especially in the neighbourhood of the inner canthus. Ramified pigment-cells are found scattered throughout the cutis vera, especially in the superficial layers around the vessels and hair-follicles (Waldeyer). Mast-cells and plasma-cells are also present normally. At the anterior border of the lid the hairs are specially differentiated to form a protection to the eyeball. The cilia are strong, short, curved hairs, arranged in two or more closely set rows. The hair-follicles are long (1·5—2·5 mm.), and pass obliquely from the anterior border towards the tarsus; they are surrounded by a dense fibrous tissue, which in the upper lid is continuous with the tarsus (Merkel). The cilia are more scattered towards the inner canthus.

The sebaceous follicles, like the cilia themselves, are specially differentiated, and are called *Zeiss's glands*. They are larger than usual, so as to supply the larger hairs which they lubricate. They are acinous glands of the usual sebaceous type.

The sweat-glands in this neighbourhood are also unusually large, and are known as *Moll's* or *modified sweat-glands*. They are situated immediately behind the hair-follicles, and their ducts open into the ducts of Zeiss's glands or into the hair-follicles themselves. The glands are tubular, lined by a single layer of cylindrical cells, the nuclei of which are near the basement membrane. The ducts are lined by a double layer of epithelial cells, the inner ones being cubical and the outer flattened. The secreting part is surrounded by a layer of unstriped muscle-fibres (Sattler), which are much better marked than those said to be present about ordinary sweat-glands (Tartuferi).

The *margin* or free edge of the lid is the part between the anterior



FIG. 1.—THE UPPER LID. × 5.

K. Position of Krause's glands. W. Position of Waldeyer's glands. H. Henle's glands. M. Meibomian glands. Z. Position of Zeiss's and Moll's glands. S.S. Sulcus subtarsalis.

and posterior borders, and has therefore been called *margo intermarginalis*. It is covered with conjunctiva, the transition taking place at the anterior border (*see* "Conjunctiva"). This border, from which the cilia spring, is rounded, whilst the posterior border, which lies in contact with the globe, is sharp. The capillarity induced by this sharp angle of contact is of importance in the proper moistening of the surface of the eye. Immediately anterior to the posterior border is a single row of minute orifices, which are just visible to the naked eye. These are the orifices of the ducts of the Meibomian glands. Between this row of puncta and the anterior border is a fine grey line, which is of importance in operations in which the lid is split, as it indicates the position of the loose fibrous tissue between the orbicularis palpebrarum and the tarsus.

The *tarsus* consists of extremely dense fibrous tissue; it contains no cartilage cells, so that the term "tarsal cartilage" is only justified in

so far as it defines the consistence of the plate. The fibrous tissue thins off imperceptibly towards the attached part of the lid into the palpebral fascia.

Embedded in the tarsus are some enormously developed sebaceous glands, the *Meibomian glands*. They consist of nearly straight tubes, directed vertically and opening by a single duct on to the margin of the lid. The tubes are closed at the upper end, and have numerous small cæcal appendages projecting from the sides, filled with glandular epithelium. The peripheral cells are cubical, staining with protoplasmic stains and containing no fat; the central cells are filled with fat globules. In young subjects the fat-free cells are more numerous, and form young terminal acini. The ducts are lined with cubical cells, but the epithelium becomes stratified at the orifices. The acini are surrounded by a lymph space lined with endothelium. The upper end of the gland is occasionally bent, and the tube may even form nearly a semicircle. The glands number from 20 to 30, being rather fewer in the lower than the upper lid.

Small groups of serous glands are not infrequently found near the convex border of the tarsus—*Waldeyer's glands* (Fuchs), or *posterior tarsal glands* (Waldeyer).[1] They resemble minute salivary glands, and are therefore similar in structure to Krause's glands (*see* "Conjunctiva").

The *orbicularis palpebrarum* consists of large bundles of striped muscle, which are cut transversely in a sagittal section of the lid; they are attached to the skin by loose subcutaneous tissue, but glide freely over the tarsal plates. The follicles of the cilia encroach upon the orbicularis, and separate off an inferior portion, which is known as the *subtarsal muscle* or *ciliary muscle of Riolan*. This consists of smaller bundles lying mostly in front of, but partly behind, the ducts of the Meibomian glands. Moll's glands separate it from the hair-follicles.

The insertion of the *levator palpebræ superioris* enters into the upper part of the upper lid. The main central band passes into the upper border of the tarsus. The anterior insertion is a flat tendinous expansion, the bundles of which pass between the bundles of the orbicularis to be attached to the skin of the middle of the eyelid. The posterior insertion into the fornix conjunctivæ does not enter into the lid proper.

The inferior rectus and oblique muscles send fibrous strands forwards into the lower lid to be attached to the tarsus and palpebral ligament.

Besides these striped muscles there is a layer of unstriped muscle in each lid. These constitute the *superior and inferior tarsal muscles of Müller*. The fibres of the upper one arise from amongst the striped fibres of the levator, pass down behind it, and are inserted into the

[1] There is much confusion in terminology here. Waldeyer calls them posterior tarsal glands, or acino-tubular glands of Krause, and says they were first represented by Klein in Stricker's 'Manual,' and described in detail by Wolfring and Ciaccio. The latter called them tarso-conjunctival acinous glands, and distinguished them from Krause's glands, which he called subconjunctival glands, a term introduced by Sappey. By Italians they are often called Ciaccio's glands. They are distinct in situation from the glands now commonly known as Krause's glands, and are much less constant. At the same time they may be merely outlying acini of Krause's glands, which are notoriously inconstant in situation. They are often inaccurately described as "mucous" glands.

upper border of the tarsus. The inferior lies below the inferior rectus, and is inserted into the lower tarsus.

The arteries of the upper lid form two main arterial arches, superior and inferior, the former lying between the upper border of the tarsus and the orbicularis, the latter in a similar position just above the hair-follicles. From the inferior one perforating branches pass down and then back between the Meibomian glands. In the lower lid there is usually only one arch near the free border, but there is sometimes a second.

There are two venous plexuses in each lid: one, post-tarsal, passing to the ophthalmic vein; the other, pre-tarsal, opening into subcutaneous veins.

The main nerves run between the tarsus and the orbicularis. A fine plexus is formed between the tarsus, orbicularis, and Riolan's muscle, constituting the *marginal plexus of Mises*. The minute distribution of the nerve-fibres has been investigated by the Golgi method by Bach.

The lymphatics are abundant; most of them pass to the pre-auricular gland, but a few from the nasal side pass along the facial vein to the submaxillary glands.

* WALDEYER.—In de Wecker and Landolt, Traité d'Ophtalmologie, i, Paris, 1886 (Bibliography, ii, p. 83). SATTLER.—Arch. f. mikr. Anat., xiii. BACH.—A. f. A., xxxiii, 1896.

INFLAMMATION

The skin of the lids is subject to most forms of dermatitis. Only those types of bacterial and parasitic inflammation which are specially important to ophthalmologists will be considered here. Variola, varicella, vaccinia, malignant pustule (anthrax), and glanders (Strzeminski) may be mentioned as occurring in this situation.

STRZEMINSKI.—Rec. d'O., 1900.

BLEPHARITIS

Blepharitis occurs in two forms—*B. squamosa* and *B. ulcerosa*. In the former there are small white scales at the edges of the lids, and the skin beneath is merely hyperæmic. The condition may be regarded as a seborrhœa (Fuchs). In *B. ulcerosa* there are yellow crusts around the hairs, and the skin is ulcerated. This condition is a true eczema. Microscopically the hair-follicles are surrounded by round-celled infiltration, with a few polymorphonuclear leucocytes. Where the skin is normal under crusts there is no blepharitis, but the crusts are due to dried conjunctival secretion.

Blepharitis ulcerosa often leads to destruction of the cilia, so that they become few, scattered, and abortive (*madarosis*), or to an alteration of their direction, owing to the contraction of cicatricial tissue (*trichiasis*), or to hypertrophy of the border of the lid, which droops owing to the weight (*tylosis*). Eversion of the border of the lid, with the punctum, may follow, due to cicatrisation pulling the conjunctiva forwards. The lids are now no longer apposed to the globe, or to each

other when shut; the tears run over (*epiphora*), the skin becomes eczematous and contracts, and so the eversion is increased, until *ectropion* is fully developed.

According to Raehlmann (2) new hair-follicles are actually developed in the intermarginal border, especially after trachoma, by down-growths of the surface epithelium.

Trichiasis must not be confused with **distichiasis**, which is a congenital condition. I have seen a case in which there were two perfect sets of cilia in each of the four lids. The inner rows irritated the cornea. Kuhnt has examined such a case microscopically. The inner row replaced the Meibomian glands, which were wholly absent. Moll's glands were hypertrophied, and there was a second row of Krause's glands in the middle of the tarsus.

Blepharitis is occasionally caused by animal parasites. *Blepharitis acarica* (Raehlmann [1]) is caused by Demodex folliculorum in the hair-follicles. In *phthiriasis palpebrarum* (or acarus) the pediculus (or phthirius) pubis, or crab-louse, occurs upon the eyelashes, which look very dark owing to the black nits which are attached to them (Chisolm). Only two cases are on record of pediculus capitis being found here, in spite of its frequency in the hair (Kraemer).

Treacher Collins has recorded an extremely rare case of **monilethrix** affecting the eyelashes and eyebrows. The hairs and cilia have a beaded appearance, the narrow parts being unpigmented. The disease runs in families, and is apparently due to periodic increased activity in the rete mucosum.

Canities or whitening of the eyelashes has been described by Nettleship, Tay, and others in sympathetic ophthalmia. It may also occur in leucoderma (Treacher Collins).

Shedding of the eyelashes is common in alopecia, leprosy, and other conditions.

RAEHLMANN (1).—K. M. f. A., xxxvii, 1899. CHISOLM.—Am. Jl. of Ophth., ix, 1892. KRAEMER.—Die tierischen Schmarotzer des Auges, in G.-S., x, 1899. RAEHLMANN (2).—A. f. O., xxxvii, 2, 1891. KUHNT.—Z. f. A., ii, 1899. TREACHER COLLINS.—T. O. S., xix, 1899. NETTLESHIP.—T. O. S., iv, 1884. TAY.—T. O. S., xii, 1892.

SYPHILIS

Both early and late manifestations of syphilis occur in the lids, but can rarely be diagnosed microscopically from other inflammations. There is the same infiltration of the tissues with lymphocytes, the same dilatation of blood-vessels and lymphatics. Endothelial proliferation, with the formation of groups of epithelioid cells, is more marked, but is not pathognomonic. There is also more extensive proliferation of the fixed connective-tissue cells, with a greater development of fibrous tissue, which is often hyaline. Giant-cells often occur, but are more often absent.

Gummata often degenerate in the centre, and, if superficial, break down upon the surface and form characteristic ulcers. They often heal with the formation of a white scar, surrounded by a pigmented zone. Subcutaneous scars show extreme fibrous tissue formation, with

very few nucleated cells. Sclerosis of the vessels is also extreme, with proliferation of the endothelium, often to the extent of obliteration of the lumen and thickening of the adventitia.

Gummata of the lids are said to be commoner in women than in men, and in the upper lid than in the lower (Hutchinson, Jr.). The necrotic process may be extreme (phagedænic), leading to partial destruction of the lids, as in a case reported by Hartridge.

Chancre of the lids has not been examined microscopically. The cases up to 1886 have been collected by de Beck. Most of them are really conjunctival, as shown by the following table:

On the cutaneous surfaces of the lids	4
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The tarsus is particularly liable to syphilitic inflammation (*tarsitis syphilitica*). It is much enlarged, so that the lid cannot be everted, and is of cartilaginous hardness. When cut into it does not bleed. Both lids of the same eye may be affected. It is a tertiary affection, which runs a prolonged course of several months. Cases have been examined histologically by Rogman, Reiner, and Basso, who found hyaline degeneration of the fibrous tissue with few nucleated cells. Near the surface the tissue was infiltrated with round-cells and partially replaced by granulation tissue, with new-formed connective tissue. In one case there were calcareous deposits (Basso). The vessels, especially the small arteries, showed hyaline degeneration, atrophy of the media, slight thickening of the adventitia, and enormous proliferation of the intima, amounting often to endarteritis obliterans. The veins suffered least. In one case, of seven years' duration, the conjunctival epithelium resembled epidermis; in another, of eight years' duration, the conjunctiva bulbi was xerotic.

Hutchinson, Jr.—R. L. O. H. Rep., xii, 2, 1888. Alexander.—Syphilis und Auge, Wiesbaden, 1889. Hartridge.—T. O. S., xviii, 1898. de Beck.—Hard Chancre of the Eyelids and Conjunctiva, Cincinnati, 1886. Rogman.—Ann. d'Oc., cxx, 1898. Reiner.—B. z. A., xxiii, 1898. Basso.—Ann. di Ott., xxix, 1900.

Lupus

In lupus the nodule consists of a delicate fibrous reticulum with numerous vessels, the larger meshes being filled with round-cells, the smaller with smaller cells and many free nuclei. Giant-cells are present in varying numbers. As the cells in the centre increase in numbers the vascular supply is interfered with, and fatty degeneration and disintegration ensue. In the epidermis the cells of the rete Malpighii undergo proliferation and fatty degeneration; there is down-growth of the interpapillary processes on the one hand, and encroachment of the lupus infiltration on the other. Similar changes occur in the epithelia of the glands and hair-follicles.

The down-growths of epithelium are occasionally very pronounced, and have led to the diagnosis of a combination of lupus and epithelioma

(lupus-carcinoma). Such a case, in which the presence of tubercle bacilli was proved by inoculation, has been described by Capauner.

These downgrowths of epithelium are common in many inflammatory conditions, and are probably only accentuated in lupus by the peculiar combination of proliferation and ulceration, granulation and cicatrisation, which here go on in such close proximity. There is no sufficient reason for regarding them as malignant in a carcinomatous sense.

Tubercle bacilli are usually present in small numbers, and can be demonstrated only with difficulty in sections. Inoculation experiments are more trustworthy.

In the later stages, and after treatment, the nodules may be absorbed, and the ulcers may completely cicatrise.

CAPAUNER.—Z. f. A., v, 1901.

LEPROSY

Leprosy occurs in two forms—the *maculo-anæsthetic* and the *nodular*. Both occur in the lids, but the latter is much more frequent.

The disease is caused by the bacillus lepræ (Hansen, 1873), which closely resembles the tubercle bacillus in staining reactions, appearance, and dimensions, though it is somewhat shorter and takes the stain more readily. Both are acid-fast, and are therefore stained by the Ziehl-Neelsen, Gabbet, and other methods. This is probably due, as shown by Bulloch and Macleod for tubercle, to a waxy constituent. In preparing films it is important not to get blood mixed with the exuding fluid, so that the nodule should be well clamped at the base with curved forceps before incision. The bacilli are variable—straight, curved, tapering or thickened at one or both ends; or they may look like a row of spores—possibly an involution form. Unlike human tuberculosis, the bacilli are found in large quantities, chiefly in groups, or bundles like bundles of cigars (Franke and Delbanco). They have not yet been successfully cultivated or inoculated, even in man (Danielssen). It is much disputed whether the bacilli are intra- or extra-cellular; they appear to be in peculiar large cells, lepra-cells (Virchow), or "globi"—possibly leucocytes enlarged by the bacilli, or glœal masses (Unna), which may be a resting stage of the parasite (Pernet). The bacilli are very widely distributed in leprous patients, and may be found in parts which show no granulomatous changes.

Most cases of nodular leprosy commence with infiltration of the eyebrows. The lids are affected relatively late (Lie), and then usually at the free edge or margo intermarginalis. Here there may be a diffuse infiltration, or a row of several small nodules, or isolated nodules, which are rarely polypoid.

Microscopically there is usually a blood or lymph vessel in the centre of the nodule, so that the bacilli are carried both by the blood and lymph streams. They are found in the intima, less frequently in intra-vascular leucocytes. The capillaries and small vessels are dilated, but there is no reaction in the surrounding tissues until the bacilli have escaped. There is then infiltration of the tissues with round-cells and moderate proliferation of the fixed cells, but even this may be absent

in the presence of extra-vascular bacilli. The reaction is much less than in tuberculosis, bacilli occurring in cells which look quite normal and may be showing active karyokinesis. The lymphoid cells become epithelioid, lepra-cells being usually in the oldest parts of the nodules, not far from the vessels (Lie). The latter become sclerosed, showing proliferation of the intima and adventitia, with little change in the media. The muscle-cells here often have pigment granules, which stain exactly like the bacilli. The nodules are always vascular, and show new formation of vessels.

Where there is no vessel in the centre of the nodule, the infiltration is often around small nerve twigs. The nerve is less attacked by the bacilli than the other tissues, so that one sees a clearer centre surrounded by a ring of connective tissue densely packed with them. They occur, however, in the perineurium, endoneurium, and in Schwann's sheath, forming long spindle-shaped aggregations in the latter. The nerves themselves often look normal, which accounts for the retained sensibility in the early stages. The growth of the nodule is always slow, but generally continuous.

The epidermis remains intact for a long time, and the subcutaneous layers are free from bacilli. Later, the infiltration reaches the rete mucosum and nutrition is interfered with, the deep cells become horny earlier than normal, and ulceration follows, with invasion of other organisms. Less often the bacilli make their way between the epithelial cells, which respond by increased mitosis. These changes also affect the hair-follicles and sebaceous glands, so that the hairs and eyelashes fall out.

There is a marked deposition of pigment granules in the rete mucosum, especially the basal layer, also to a less extent in the connective-tissue cells, but not so much here as in the muscle-fibres of the arrectores pilorum. The cells of the sweat-glands are also markedly pigmented, though rarely invaded by the bacilli, contrasting in this respect with the sebaceous glands and hair-follicles.

The "globi" consist of masses of bacilli, and may be so large as to appear as fine points to the unaided eye in stained preparations, a fact which seems incompatible with their being contained in cells (Lie).

DANIELSSEN AND BOECK.—Traité de la Spedalskhed, Paris, 1848. BULL AND HANSEN.—The Leprous Diseases of the Eye, London, 1873. UNNA.—Histopathology, London, 1896. * BORTHEN AND LIE.—Die Lepra des Auges, Leipzig, 1899. FRANKE AND DELBANCO.—A. f. O., l, 2, 1900. BABÈS.—Die Lepra, ii, 1901.

RINGWORM, FAVUS

Ringworm of the eyelids and eyelashes has been frequently observed; it calls for no special mention here.

Only a few cases of favus of the lid are on record, but its occurrence is probably more frequent than the paucity of reported cases would lead one to expect. The disease commences with the formation of yellowish-red vesicles, and rapidly goes on to the formation of a bright yellow crust, which is very characteristic. I have examined one case, and there was no difficulty in demonstrating the Achorion Schönleinii. The patient's cat was also examined, but without result, though the

source of the disease in cats or mice has been almost certain in some cases (MacHardy, Quincke, Pick).

NARKIEWICZ-JODKO.—K. M. f. A., viii, 1870. SCHIESS-GEMUSEUS.—K. M. f. A., xi, 1873. MACHARDY.—T. O. S., v, 1885. QUINCKE.—Monatsheft f. Derm., vi, 1887. PICK.—A. f. Derm., 1891. LIBMAN.—A. of O., xxvii, 1898. GLOOR.—A. f. A., xxxvii, 1898. TREACHER COLLINS.—T. O. S., xxiii, 1903.

XANTHELASMA—XANTHOMA

Xanthoma palpebrarum occurs almost always in plates (*X. planum*), but occasionally in nodules (*X. tuberosum*). It usually commences on the inner canthus of the left upper eyelid, and may form a semicircle round the eye by the coalescence of patches. Sooner or later similar patches occur on the right side, the disease always becoming symmetrical. The plates are embedded in the corium, very slightly or not at all raised above the surface, yellow, soft and smooth to the touch. With a lens the patches can often be seen to consist of small yellow granules, with a central pinkish punctum.

It occurs at ages from twenty to eighty-four (Hutchinson), usually over forty; is more common in females than in males; occurs in families, and may be hereditary. Half of Hutchinson's cases suffered from migraine; one sixth had had jaundice, but this is commoner in X. multiplex (Radcliffe-Crocker).

Microscopically the changes are chiefly in the middle and lower layers of the corium, and consist in aggregations of large epithelioid, multinucleated, oval, round, or polygonal, finely granular cells, lying in a fine meshwork of connective tissue, and separated from one another by bands of connective tissue. The cells form irregular masses, or whorls and nests, this arrangement being due to their formation round a blood-vessel. Yellowish-brown pigment is scattered about within and amongst the cells, and also in the cells of the rete Malpighii, a large number of which are vacuolated. The xanthoma cells undergo fatty degeneration and seem to run together, so that their contour is indistinct. They may at first be spindle-shaped, but later are pressed together like epithelial cells.

The origin of the cells is doubtful. The majority of authors think they are connective-tissue cells, the changes occurring most where these are most numerous, viz. near the vessels, nerves, glands, and hair-follicles, and this leads to the granular arrangement. They have also been derived from endothelial cells (endothelioma lipomatodes). They were early derived from sebaceous glands, but this is inaccurate (Waldeyer). Unna considers that the fat is not in the cells, but in lymph spaces, and that the nuclei are free in it. Pollitzer traced the cells to degenerated muscle-fibres.

The fat is rather an infiltration than a degeneration, the nuclei staining well. In sections obtained by freezing, and kept in glycerine, it crystallises in long needles.

Dessauer says that the same clinical picture can result merely from hypertrophy and increase of sweat-glands with cystic degeneration, but this requires confirmation.

RADCLIFFE-CROCKER.—Diseases of the Skin, London, 1903. HUTCHINSON.—Med.-Chir. Trans., liv, 1871. XANTHOMA COMMITTEE.—Trans. Path. Soc., xxxiii, 1882. WALDEYER.—Virchow's Arch., lii, 1871. PYE-SMITH.—Guy's Hosp. Rep., 1877. UNNA.—Histopathology of Diseases of the Skin, London, 1896. POLLITZER.—New York Med. Jl., 1899. DESSAUER.—A. f. O., xxxi, 3, 1885. ALT.—A. of O., viii, 1879; Am. Jl. of Ophth., xiii, 1896.

INFLAMMATION OF THE GLANDS OF THE LIDS

Hordeolum, or Sty, occurs in two forms, H. externum and H. internum.

Hordeolum externum is a suppurative inflammation of one of Zeiss's glands. It is usually caused by staphylococci.

Hordeolum internum or Meibomianum is a suppurative inflammation of one of the Meibomian glands. Owing to the firm tissue in which the gland is embedded, the inflammation is more severe and more prolonged. The abscess opens through the gland duct or on to the conjunctival surface. The inflammation is due to staphylococci, and may spread to the surrounding tarsus and lead to considerable necrosis (*tarsitis necroticans*) (Mitvalski). Maklakoff reports a case of chronic purulent inflammation of the Meibomian glands, in which *Bacillus mucosus ozænæ* was found. It was also found in the nose. The pus exuded from the duct-openings, and the condition had existed for five years.

CUÉNOD.—Bactériologie et Parasitologie clinique des Paupières, 1894. FUCHS.—K. M. f. A., xvi, 1878. MITVALSKI.—C. f. A., xxi, 1897. MAKLAKOFF, JR.—A. f. A., xliii, 1, 1901.

Chalazion is a chronic inflammatory affection or granuloma of a Meibomian gland. The older observers regarded it as an hordeolum which had not gone on to suppuration. Others considered it a simple retention cyst. These do occur, *e.g.*, in trachoma (q. v.), but are essentially different from chalazia.

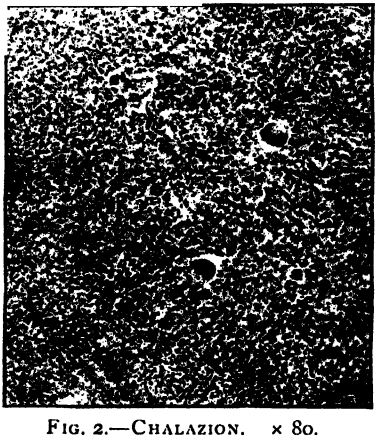


FIG. 2.—CHALAZION. × 80.

The section shows granulation tissue, containing blood-vessels, with two giant-cells of the Langhans type.

In a chalazion there is a peculiar chronic inflammation which produces granulation tissue containing giant-cells (Fuchs) (Fig. 2). de Vincentiis called it a *granuloma giganto-cellulare.* The epithelium of the acinus first proliferates without forming fatty sebaceous material, so that the cytoplasm stains well. The acinus becomes swollen and forms club-shaped expansions. The central fatty cells are imprisoned, and break down into granular amorphous flakes. The surrounding tissue of the tarsus is densely infiltrated with lymphocytes, and the fixed cells proliferate. This process soon becomes the predominant one, so that both the acini of the gland and the periacinous tissue are ultimately lost in a mass of granulation

tissue. This contains giant-cells, which are said to be derived both from the glandular epithelium and from the endothelium of the peri-acinous tissue. According to Krause, the surrounding infiltration is the primary phase. According to Fuchs, the glandular changes are primary, and he compares it to a desquamative catarrh following prolonged or repeated inflammation of the conjunctiva or lid-margin. The inflammatory process either extends up the ducts of the glands, or leads to obliteration of their mouths.

The growing tumour presses more and more upon the surrounding tissue, which becomes compressed, and forms a connective-tissue capsule. This is least developed in the direction of least resistance, which is usually towards the conjunctival surface, and here the granulation tissue extends, and finally breaks through.

The chalazion is poor in vessels, proliferation taking place chiefly at the periphery. The centre contains remnants of glandular tissue, infiltrated with cells, lying in fibrous tissue which has few cells. The fibrous development probably leads to retrogressive changes in the blood-vessels, and the central parts degenerate. The fibres become hyaline and fuse into a fluid homogeneous mass; the cells become vacuolated and finally disappear. The tissue does not give the reactions of mucin, and is therefore not a true myxomatous degeneration. The giant-cells also degenerate, so that they are more numerous in the early than in the later stages. In old chalazia the entire contents may be liquefied and may form a cyst, with a thick fibrous wall, containing turbid gelatinous fluid.

Bacteriology.—At a time when the Langhans type of giant-cell—with the nuclei arranged around the periphery or at the poles—was regarded as pathognomonic of tubercle, chalazion was naturally included in this category. It is now known that the ordinary irritation, or foreign-body giant-cell (Fremdkorperriesenzell), may be of the Langhans type. Moreover material from chalazia inoculated into the anterior chamber of rabbits does not produce tuberculosis (Weiss, Deutschmann, Landwehr, etc.), though when placed in the peritoneal cavity of guinea-pigs it may cause death (Parisotti). v. Wichert considered twenty-eight out of thirty-two chalazia tuberculous on anatomical grounds, though bacilli were only found twice, and inoculations failed. At the same time it seems probable that in exceptional cases chronic tuberculosis of the tarsus may show the clinical picture of chalazion (v. Michel, Tangl, and v. Wichert), and ordinary chalazion in tuberculous subjects may contain tubercle bacilli (Tangl). Inoculation of dead tubercle bacilli will not produce the complaint (Deyl). Palermo produced tubercle of the tarsus by inoculation in rabbits, but it led to ulceration and even death, but no evidence of chalazion. He regards the condition as a foreign-body granuloma, in which chemical, physical, or bacterial irritation may play a part, leading to a desquamative catarrh, with adenitis and periadenitis.

Specific organisms have been described. Poncet and Boucheron, confirmed by Lagrange, found cocci which stained by Gram; they were of unequal size, and were possibly nuclear fragments (Uhthoff and Axenfeld).

Deyl found bacilli invariably in fresh chalazia (chalazion bacilli). He admits their morphological and cultural identity with xerosis bacilli. Hála found them in large numbers in young chalazia only. They gradually dwindle, so that in four or five weeks they are absent. They are short thick rods with rounded ends, one usually thicker than the other; in the later stages they are larger, and show more segmentation. In common with Uhthoff and Axenfeld and others, he regards them as xerosis bacilli.

Priouzeau found staphylococci, diplobacilli, Friedländer's pneumobacilli, streptococci, tetragenus, leptothrix; he considers staphylococci causal. He is strongly in favour of the infectious nature and transmissibility of the disease, both on insufficient grounds.

DE VINCENTIIS.— Della Struttura e Genesi del Chalazion, etc., Naples, 1875. FUCHS.—A. f. O., xxiv, 2, 1878. KRAUSE.—Inaug. Diss., Berlin, 1891. WEISS.—K. M. f. A., xxix, 1891. DEUTSCHMANN.—B. z. A., ii, 1891. LANDWEHR.—Ziegler's Beiträge, xvi, 2, 1894. PARISOTTI.—Internat. Congress in Rome (*see* C. f. A., xviii, 1894). V. WICHERT.—Nauwerck's Path. Anat. Mittheil., xv, 1894. DEYL.—Acad. des Sciences, Prague, 1893-4. PALERMO.—Ann. di Ott., xxvi, 1896. HÁLA.—Z. f. A., vi, 1901. PRIOUZEAU.—Ann. d'Oc., cxix, 1898. * UHTHOFF AND AXENFELD.—In Lubarsch and Östertag, 1894, 1895-6, 1897-8-9. HENKE.—Deutsch. path. Gesellsch., iv, 1902.

HYPERTROPHIC AND ATROPHIC CONDITIONS

HYPERTROPHIC CONDITIONS

Hypertrophic conditions of the lids are not always easy to distinguish from some tumours, *e. g.* lymphomata, lipomata, etc. They are often associated with orbital affections. They occur typically in elephantiasis and myxœdema.

In **elephantiasis lymphangioides** and **elephantiasis Arabum** the condition is due to lymph stasis. Several cases have been collected by Becker. The changes are chiefly in the subcutaneous tissue, which is enormously hypertrophied from increase of fibrous tissue, mostly in bands or networks, other parts being gelatinous, with soft fine fibres, and many nuclei and cells. The blood-vessels and lymphatics are enormously enlarged, and the muscles show fibro-fatty changes. The epidermis is also proliferated.

BECKER.—A. f. O., xli, 3, 1895. KÖNIGSHOFER.—Ophth. Klinik, 1902.

Allied to elephantiasis are the cases of **chronic œdema** which are occasionally met with. Their pathology is obscure, and the tissues have seldom been submitted to microscopic examination. In a case following erysipelas, Rombolotti found œdema of the subepithelial tissues, with dilatation of the lymph spaces. There was some round-celled infiltration, and marked hyperplasia of the fixed-tissue elements. The dilatation of the lymph spaces was less marked than in Polignani's case.

POLIGNANI.—Lav. della Clin. Oc. di Napoli, iii. ROMBOLOTTI.—A. f. A., xxxvi, 1898. ANDERSON CRITCHETT.— T. O. S., xix, 1899.

The upper lid is a favourite situation for **elephantiasis neuromatodes** or **neuro-fibromatosis.** Cases have been reported by Billroth, Bruns, etc. There is the characteristic hypertrophy of the nerves, and also a condition of lymph stasis and fibromatosis of the subcutaneous tissues. The condition of the lid in the case reported by Rockliffe and myself was as follows:

The upper lid was enormously swollen, the increase in tissue being principally upon the posterior or conjunctival side, resulting in marked ectropion (Fig. 3). This increase of growth consisted of masses of convoluted nerves covered by inflamed conjunctiva. The nerves were generally smaller than those in the major orbital part of the growth, but showed similar hypertrophy of the endo- and peri-neurium. The



FIG. 3.—PLEXIFORM NEUROMA. × 3.

From Parsons and Rockliffe, Trans. Path. Soc., liv. Showing ectropion, due to hypertrophy of nerves in the posterior part. Note the subconjunctival infiltration and the dilatation of lymph spaces in the anterior layers.

nerve-fibres, stained by Weigert's method, showed comparatively little change. The other tissues of the lid exhibited more œdema and congestion, great dilatation of the subdermal lymphatics being a marked feature.

The subject of plexiform neuroma will be discussed more in detail in treating of orbital tumours.

PARSONS AND ROCKLIFFE.—Tr. Path. Soc., lv, 1904. DE SCHWEINITZ.—T. Am. O. S., 1891.

The lids are always affected in **myxœdema.** There is thickening and degeneration of the elastic tissue, and in less degree of the white fibrous tissue. There is usually little cellular infiltration. The epithelium of the sebaceous and sweat-glands becomes swollen in the early

stages, and degenerates later. The root-sheaths of the hairs show irregular protrusions, probably due to constriction by an excess of surrounding fibrous tissue. Degeneration of the hair-follicles leads to shedding of the hairs (Fig. 4). The arterioles also show thickened fibrous coats (Fig. 5) (Ord). Halliburton failed to find any appreciable increase of mucin in the skin in myxœdema.

Ord.—Med.-Chir. Trans., lxi, 1877. *Committee on Myxœdema.—Trans. Clin. Soc., xxi, Suppl., 1888.

Hypertrophy of the tarsus alone, and even ossification, may occur, as in a case reported by Herbert. Calcification in the conjunctiva

Fig. 4.



Fig. 5.

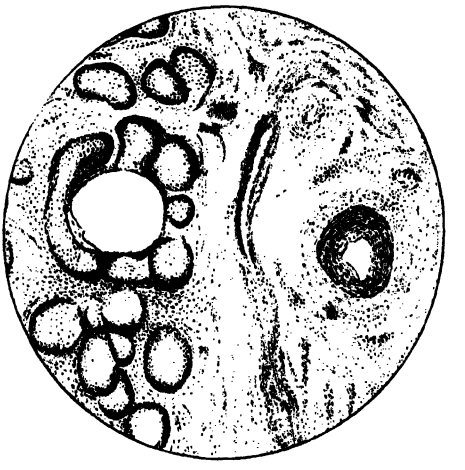


Fig. 4.—Myxœdema. × 50.

After Orr, Med.-Chir. Trans., lxi. Showing thickening of the fibrous walls of the hair-follicles, and irregular bulging of the root-sheath, either due to budding from its surface or constriction by surrounding fibrous tissue. The hairs are in process of being shed.

Fig. 5.—Myxœdema. × 50.

After Orr, Med.-Chir. Trans., lxi. Showing Meibomian glands and arterioles, with thickened fibrous coat.

tarsi is not uncommon in natives of India, according to this observer. (*Cf.* "Conjunctivitis petrificans.")

Herbert.—T. O. S., xxi, 1901.

Atrophic Conditions

In **senile atrophy** there is degeneration of both elastic and white fibrous tissue (Unna). The former is broken up into granules and globules, which stain with elastic tissue stains (Weigert's, acid orcein). Small nodules of lymphocytes are common. The hair papillæ are shrunken, with cornification of the outer root-sheaths; the sebaceous glands are enlarged.

In **blepharochalasis** (Fuchs) the skin of the upper lid becomes so thin that it lies in countless little wrinkles. It occurs at all ages in cases in which there have been frequent antecedent œdematous swellings, *e. g.* after recurrent neurotic œdema. The small superficial veins are dilated. Anatomically there is atrophy in all parts—the papillæ are much flattened or have disappeared; the subcutaneous tissue is loose, consisting of finer fibres with wider meshes than normal; the elastic tissue is finer and more discrete (Fehr).

Fuchs.—Wien. klin. Woch., 1896. Fehr.—C. f. A., xxii, 1898.

Atrophy of the tarsus occurs in trachoma (q. v.).

TUMOURS

Molluscum Contagiosum

Molluscum contagiosum occurs not very commonly as a small, firm, hemispherical, umbilicated tumour, at first sessile and waxy-looking, later opaque yellow and pedunculated.

In vertical section the tumour consists of wedge-shaped lobules,



Fig. 6.—Molluscum Contagiosum. × 55.

The section shows a typical tumour, with the epithelium arranged in loculi. The transition of the cells to "molluscum bodies," and their extrusion into the orifice, are seen.

separated by thin fibrous septa, and enclosed, except on the surface, by a fibrous capsule (Fig. 6). The border is continuous with the

epidermis, each lobule is bounded by palisade epithelium, and round nucleated epithelial cells adjoin this. These cells show various stages of molluscous degeneration, those near the surface being most advanced. This consists of a hyaline degeneration, with enlargement of the cell, until it finally forms a homogeneous mass or *molluscum body*. These bodies, which do not stain with ordinary dyes, accumulate at the mouth of the lobule, and the tumour may be emptied by squeezing them out.

It was formerly thought that the growth consisted of altered sebaceous glands. The degeneration is now generally considered to be in the prickle-cells of the upper (Thin) or lower (Radcliffe-Crocker) layers of the rete. Charles J. White says that the material is not hyaline or colloid substance, but normal keratin, reacting like corneous epithelioma to polarised light (Piffard).

A unique case of molluscum contagiosum of the bulbar conjunctiva has been recorded by Ballaban.

Salzer records the case of a lady with molluscum contagiosum, in which it seemed probable that she had contracted it from pigeons; these had growths on the beak, said to be epithelioma contagiosum of fowls. Shattock has seen molluscum contagiosum in bunting.

The disease is probably due to an organism. Psorosperms were invoked, but found few supporters. Robey found only the *Staphylococcus epidermidis albus* of Welch.

RADCLIFFE-CROCKER.—Diseases of the Skin, London, 1903. WHITE AND ROBEY.—Jl. of Med. Research, vii, 1902. *MUETZE.—A. f. A., xxxiii, 1896. BALLABAN.—A. f. A., xlvii, 1903. SALZER.—Münch. med. Woch., 1896; Brit. Jl. Derm., ix, 1897. SHATTOCK.—Tr. Path. Soc., xlix, 1898.

VERRUCA

Warts occur upon the lids and the lid margins, especially the senile form (V. senilis or keratoma senile). They are usually flat, soft or hard according to the amount of corneous change, often multiple.

Senile warts are often multiple. They show little papillary proliferation, but often downgrowths of plugs of epithelium. These do not necessarily prove malignancy, but it is certain that these warts are liable to degenerate into epithelioma or rodent ulcer. On the other hand, they not infrequently fall off spontaneously. The epithelium is usually thickened, with a moderate increase in the horny layers; the cells are often pigmented.

CORNU CUTANEUM

Cutaneous horns grow rarely on the lids or their edges. They are usually solitary, conical with rounded apices.

The papillæ at the base are usually hypertrophied, and extend upwards a short distance into the horn, stopping sooner in the axis than at the periphery (Fig. 7). The essential change, however, is in the prickle-cells, which proliferate rapidly, the young cells quickly

becoming horny without being shed. They thus accumulate and form the main mass of the growth. The horny cells are arranged in columns of concentric laminæ, with similar cells irregularly placed in the interstices, cementing them together. The hair-follicles and ducts of the sweat-glands participate in the epithelial proliferation.

That the condition is dependent upon epithelial, and not papillary proliferation (Unna), is shown by the growth of horns where there are no papillæ, *e. g.* on a cicatrix (Bland-Sutton), on the cornea of a cow (Baas), on a staphylomatous pseudo-cornea (Arnold Lawson). These cases, however, are open to different interpretation (*see* "Cornea").

MITVALSKI.—Arch. f. Derm., xxvii, 1894. BLAND-SUTTON.—Tumours, London, 1902. BAAS.—C. f. Path. u. path. Anat., viii, 1897. LAWSON.—T. O. S., xx, 1900.



FIG. 7.—CUTANEOUS HORN. × 16.

The "horn" was removed from the edge of the lid. The papilloma-like base is seen, and the masses of adherent corneous scales. The base is composed of vascular fibrous tissue covered by epidermis, the inner boundary of which is faintly visible.

FIBROMA

Fibromata of the lids are usually soft and polypoid, the surface being smooth or papillary. The fibrous tissue varies greatly, being often gelatinous in the smallest tumours, coarse and compact in the larger ones, frequently with hyaline degeneration. The tumours are usually richly supplied with blood-vessels, which often give rise to hæmorrhages, resulting in pigmentation with blood pigment. All the cells may become pigmented, besides the normal chromatophores in the sub-epidermal layers. Mast-cells are present in large numbers, and Unna describes a special type as the most striking constituent; with polychrome methylene blue they show a dense oval halo, staining red, and about double the size of the contained mast-cell with its small blue nucleus.

Owing to their shape and exposed situation, fibromata are liable to injury, resulting in the hæmorrhages already mentioned and inflammatory reaction. They may then show marked vascular congestion, with increase of intra-vascular leucocytes, and dense infiltration with round-cells.

Rumschewitsch has described a *myxoma* of the upper lid, which was probably only an œdematous fibroma.

Many fibromata are in reality neuro-fibromata (*molluscum fibrosum*) forming polypoid tumours, having the same structure as diffuse neuro-fibroma.

RUMSCHEWITSCH.—K. M. f. A., xxviii, 1890.

Lipoma

The skin of the lid is peculiar in having no adipose tissue; hence lipomata of the lid are probably always secondary extensions from the orbit. These are generally congenital fibro-fatty tumours (*see* "Conjunctiva"), which may send processes under the skin, usually running between the muscles and the tarsus.

Vossius published a case which he regarded as a true lipoma of the upper lid; others have been diagnosed, but with scanty and insufficient details.

Wingenroth published a remarkable case of symmetrical tumours in all four eyelids of a woman æt. 50. They consisted of myxomatous tissue, with large star-shaped cells, and with isolated and aggregated fat-cells. There were multiple lipomata over the body. The author regarded the tumours as lipomata with myxomatous degeneration, though the possibility of elephantiasis or of multiple neuro-fibromata received consideration. In any case it is doubtful if the tumours were true primary growths of the lids.

Vossius.—B. d. o. G., 1895. Wingenroth.—A. f. O., li, 2, 1900.

Angioma

Angiomata arise from the blood-vessels—hæmangiomata,—and from the lymphatics—lymphangiomata.

Hæmangiomata are either capillary or cavernous. Capillary hæmangiomata are either congenital (*capillary nævi*) or acquired (*telangiectasis*). In either case they consist of capillaries, increased in size and number, and closely aggregated. *Cavernous nævi* are circumscribed and composed of thin-walled veins and sinuses, bound together by a small amount of cellular connective tissue. The walls often consist simply of endothelium lying on the connective tissue. A few small arteries open into the sinuses without the intervention of capillaries.

Lymphangiomata can only be diagnosed microscopically from hæmangiomata when the spaces contain no blood. The lymph usually appears in sections as granular coagulum containing a few lymphocytes, or as a homogeneous hyaline material. Often, however, the diagnosis is impossible in the absence of the clinical appearances, as blood enters the spaces during the operation for removal (*see* "Conjunctiva").

Lymphoma

Lymphomata are small round-celled tumours, which often cannot be distinguished histologically from small round-celled sarcomata. Many of them belong to those indeterminate cases which also offer great difficulties in clinical classification, and are variously described as lymphoma, lymphadenoma, lympho-sarcoma, etc. They occur in the lids and orbits, being often symmetrical, and not infrequently involving all four lids. Hochheim divides them into four groups:

1. *Simple lymphomata.*—Most cases reported are orbital, *e. g.* Silcock's.

2. *Leukæmic tumours* in patients suffering from leukæmia. They were found in all four lids, under the skin, in a case of Leber's; between the conjunctiva and tarsus in a case of Birk's; most are orbital.

3. *Pseudo-leukæmic tumours*, usually in anæmic patients, the type of anæmia varying or being insufficiently investigated. Bronner reports a case involving all four lids, and other lid cases are quoted from Guaita, Axenfeld, Dutoit, etc.; most are orbital.

4. Doubtful cases.

The diagnosis of these cases depends entirely upon clinical details. Histologically they are all tumours composed of masses of small round-cells, resembling lymphocytes, lying in a fibrous reticulum, which often forms a definite stroma between the individual cells. They are not usually encapsuled, but the neighbouring muscles, etc., are infiltrated with lymphocytes. There is often endothelial proliferation, and sometimes an excess of eosinophile corpuscles. Their vascularity varies.

Lymphoma has been used as a generic term for follicular conjunctivitis, trachoma, etc., by Reid, an example which should not be copied, as it leads to the confusion of very different conditions, which are gradually being differentiated.

*Butlin and others.—Discussion on Lymphadenoma, Tr. Path. Soc., liii, 1902. Silcock.—T. O. S., viii, 1888. Leber.—A. f. O., xxiv, 1, 1878. Birk.—St. Petersburger med. Woch., 1883. Bronner.—International Congress, Edinburgh, 1894. Meller.—A. f. O., l, 1, 1900. *Hochheim.—A. f. O., li, 2, 1900. *Dutoit.—A. f. A., xlviii, 1903.

Sarcoma

Reported cases of primary sarcoma of the lids are rare, but probably afford little idea of its relative frequency. Wilmer (1894) collected thirty-five cases, Veasey (1899) added thirteen, and Friedenwald (1900) six more. Wilmer found the age of the patients to vary from ten months to seventy-six years; the size varied from that of a pea to a large apple. In 12 per cent. all four lids were involved. In 40 per cent. recurrence is reported; but the numbers are too few to admit of accuracy in percentages.

The growth may arise from any structure in the lid except the epithelium. Many spread from the conjunctiva; some originate in pigmented nævi (Hohemberger); but these would now be classified differently by many (*see* "Conjunctiva"). It is probable that some are in reality primarily orbital.

Histologically all types of sarcoma are represented: round-celled (43 per cent., many of which are doubtful—*v.* "Lymphoma"); spindle-celled (40 per cent., more probably the majority); mixed-celled (17 per cent.); myxosarcoma (11 per cent.). Multinuclear cells resembling giant-cells may occur, as in many sarcomata other than true myeloid. Angiosarcomata and alveolar sarcomata also occur, and are probably endotheliomata. Probably about half the cases are pigmented.

Wadsworth and Verhoeff have reported a case of leucosarcoma of the lower lid associated with a melanotic sarcoma of the limbus; the tumours were in contact. The only other similar case seems to be that of Szulislawski.

VAN DUYSE AND CRUYL.—Ann. d'Oc., xcviii, 1887; ci, 1889. HOHEMBERGER.—A. f. O., xxxviii, 1892. *WILMER.—T. Am. O. S., 1894. SZULISLAWSKI.—C. f. A., xx, 1896. FAGE.—A. d'O., xvii, 1898. VEASEY.—T. Am. O. S., 1899. CAPELLINI.—Ann. di Ott., xxviii, 1899. FRIEDENWALD.—T. Am. O. S., 1900. DE BERARDINIS.—Ann. di Ott., xxix, 1900. WADSWORTH AND VERHOEFF.—T. Am. O. S., 1901. WORK DODD.—T. O. S., xxiii, 1903.

ENDOTHELIOMA

Endotheliomata are said to be common in the lid. They are tumours which start in the endothelium of the blood or lymphatic vessels. There can be no doubt that such tumours form an important class, and, when typical, are not difficult to differentiate from other sarcomata or from epitheliomata. On the other hand, endothelial proliferation is common in many tumours and granulomata, whilst the



FIG. 8.—MELANOTIC SARCOMA OF LID. × 13.

From a girl æt. 17. Small "mole" noticed six or seven years. The growth infiltrates the whole of the lid border, and large pigmented cells extend up along the conjunctiva and Meibomian ducts. The cells vary in size and shape, show a tendency to alveolation in places, and probably arose from a congenital nævus.

endothelium in many endotheliomata is said to so alter that the cells become spindle-shaped, asteroid, etc., and they cannot be distinguished from embryonic connective-tissue cells. How far this is true may be held open to doubt in the present state of knowledge. I consider that the term endothelioma is useful where the origin from endothelium can be demonstrated or is reasonably probable; but where great metaplasia (v. Hansemann), or change in the form of the cells, is supposed to have occurred, resulting in atypical forms, I think the term is better avoided, the growths being called sarcomata, according to the old nomenclature. Only a false idea of certitude is arrived at by dogmatic nomenclature, and the effect is to retard precise knowledge. Hinsberg considered

four out of eight epitheliomata of the lid to be endotheliomata, and Ginsberg three out of six; these are probably examples of enthusiasm outrunning discretion. The subject will be dealt with more fully in considering sarcomata of the choroid.

v. HANSEMANN. — Die mikr. Diagnose der bösartigen Geschwülste, Berlin, 1897. HINSBERG.—Beiträge zur klin. Chirurgie, xxiv, 1899. GINSBERG.—Grundriss der path. Histologie des Auges, Berlin, 1903.

EPITHELIOMA

Epithelioma is one of the commonest tumours of the lids. As elsewhere, its favourite site is the meeting place of different kinds of epithelium, so that it commences most frequently at the lid margin, usually of the lower lid.

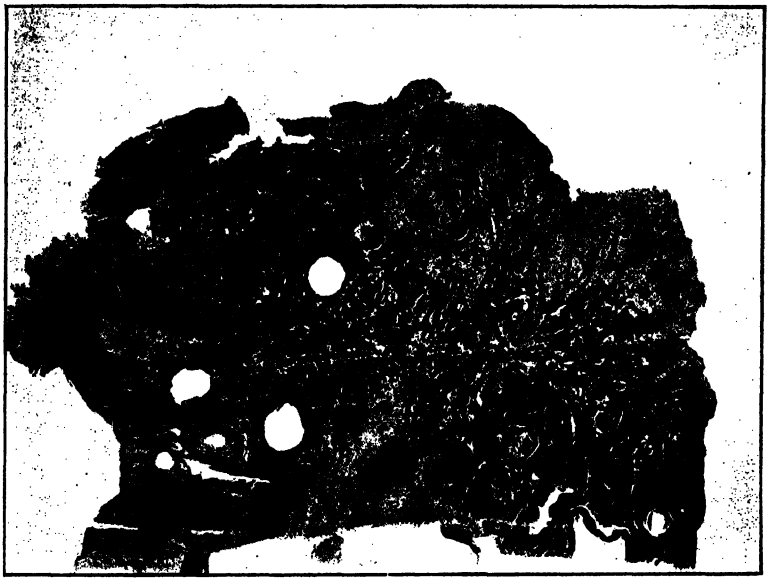


FIG. 9.—EPITHELIOMA OF LID. × 14.

This is a general view to show the downgrowing processes of epithelium. Some can be seen to fade off imperceptibly into the underlying stroma, which is densely infiltrated with round-cells. "Cell-nests" are seen, but some of these have dropped out, leaving spaces.

Microscopically there is great downgrowth of the interpapillary processes of the rete, and secondary processes bud off from these laterally as well as terminally, and anastomose, forming a coarse epidermal network (Fig. 9). Buds may also come off from the hair-follicles, and probably from the sweat and sebaceous glands, but this is doubtful. It is generally held that the epidermal epithelium invades the corium by proliferation, but some pathologists consider that an "infective" activity transforms the connective-tissue cells into epithelial cells. It is certain that in many places, particularly at the ends of the

growing plugs, the distinction between epithelial and connective-tissue cells is to a large extent lost, and it is impossible to say of some cells in this area to which category they belong. Here the basement membrane is entirely lost, and these features are of extreme importance in settling the question of malignancy and discriminating between epithelioma and benign epithelial proliferation with down-growth, such as occurs in many warts and inflammatory conditions—notably, however, in the conjunctiva. Another point of importance is the condition of the connective-tissue stroma between the plugs. The cancerous epithelium exerts an irritating influence upon the tissues, which respond by inflammatory infiltration. The stroma becomes packed with lymphocytes, which separate and break up the fibres; the tumour may disintegrate or slough from obliteration of the vessels, induced by pressure of the epithelium and leucocytes, aided by endarteritis. This inflammatory infiltration is usually absent in benign growths, but I have seen it in a case of papilloma which had been treated with glacial acetic acid.

The epithelial plugs retain to a large extent the structure of the epidermis, having cylindrical cells at the periphery; prickle-cells, often particularly large and well-developed, within; and in the centre stratified horny cells. The latter are often compressed into cell-nests, with laminæ like the layers of an onion; there are often multinucleated cells in the centre, and "colloid" cells are sometimes found. Cell-nests are also found free in the stroma. They are not pathognomonic of epithelioma.

The stroma and its vessels never invade the epithelial plugs, but polymorphonuclear leucocytes are often found between the epithelial cells. The latter sometimes show vacuolation, the nuclei being pressed to one side. Degenerative changes are most marked in the middle of the plugs, and the cells may here break down into a granular or striated coagulum, which stains deeply with hæmatoxylin and probably contains mucin. In this manner gland tubes may be simulated. The surface of the growth commonly degenerates, forming a malignant ulcer.

Hutchinson has described a *crateriform ulcer* which much resembles rodent ulcer and affects the same regions, but is microscopically an epithelioma. It occurs as a bossy lump with a conical summit, which later ulcerates.

Mayeda has recently investigated the subject of malignant epithelial growths of the lid, and has seen reason to believe that epithelioma is less common than the glandular type of carcinoma (*v. infra*).

PURTSCHER.—A. f. A., x, 1881. HUTCHINSON.—Trans. Path. Soc., xl, 1889. MAYEDA.—B. z. A., lvi, 1903.

RODENT ULCER

The lids and sides of the nose are favourite situations for rodent ulcer.

Most Continental writers regard this growth as a variety of epi-

thelioma, a view supported by Hutchinson and others in England. Others believe it starts from the sebaceous glands (Thiersch, Butlin), from the sweat-glands (Thin, Norman Walker), or from the hair-follicles (Bowlby and others). It is generally agreed in England that it is a subepidermal growth with the structure of a glandular cancer, and quite distinct from squamous-celled epithelioma. As a late event the rete may be involved, but unless this happens the greater part of the growth is made up of granulation tissue, the epithelial proliferation being comparatively moderate (Radcliffe-Crocker).

The cells of rodent ulcer are smaller than ordinary epithelial cells, and occur in irregular masses and bands beneath the epidermis or ulcerated surface (Fig. 10). The outer cells are usually more or less



FIG. 10.—RODENT ULCER. × 60.

The section is to the right of the ulcerated surface, and shows the skin being undermined. Note the columnar arrangement of the peripheral cells of the neoplasm. Between the epidermis and the growth is a layer of infiltrated hyaline connective tissue, with dilated blood-vessels.

cylindrical, with their oval nuclei arranged with the long axis perpendicular. Thin gives the following distinguishing features:—In rodent ulcer the nucleus of the cells is fairly uniform in size, the cell protoplasm is scanty and not granular, and the cell-wall is not discernible; further, the cells never enlarge into the flat horny cells of epithelioma, they never become prickle-cells, never form nests, do not retain the dye of eosin, soften in the centre of the cell masses by mucoid degeneration, and the cell infiltration and disorganisation of the corium are much less than in epithelioma, while the cell infiltration and mitoses do not go far beyond the cell growth.

Tumours of the rodent-ulcer type are probably much commoner

in the lids than true epitheliomata. My experience in this respect agrees with that of Mayeda. Between the two extremes—themselves not very far apart—of typical epithelioma and typical rodent ulcer, there are tumours which show characteristics of each, but are on the whole more nearly allied to the glandular type of carcinoma (Fig. 11). In these the cells are cylindrical at the periphery, oval or spindle-shaped, and irregular at the centre. They are arranged in columns, within which the individual cells may form rosette-like groups, sometimes with a lumen, which may contain secretion. There may be large nests of cells with a central cavity, but cornification of the cells is absent. The growths seldom extend deeply into the tissues, and have the prolonged course of rodent ulcer. Often

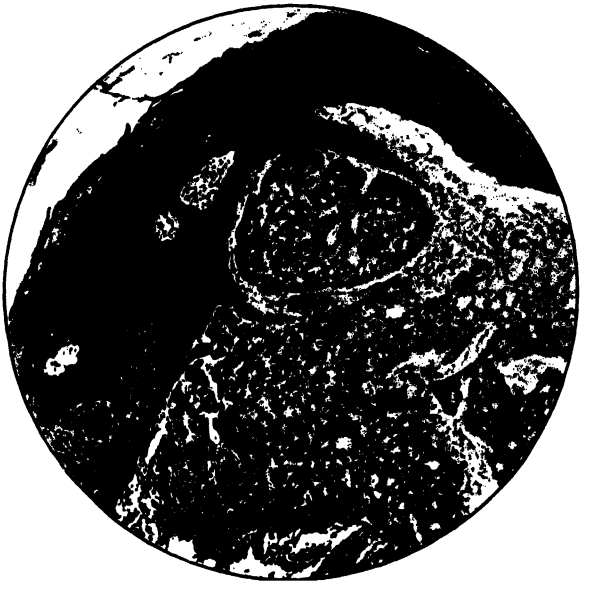


FIG. 11.—RODENT ULCER OF LID. × 60.

This part of the section shows a somewhat alveolar arrangement, strongly indicating the origin of the growth from glandular tissue. In the lower part there is round-celled infiltration. Other parts of the growth showed the more usual characteristics of rodent ulcer.

the sebaceous glands and hair-follicles around the growth are connected with it by strands of carcinomatous cells. Most of the tumours are certainly independent of the Meibomian glands, but it is most likely that they originate in the glands of the skin.

BOWLBY AND OTHERS.—Path. Soc. Trans., xlv, 1894. THIN.—Cancerous Affections of the Skin, London, 1886. *MAYEDA.—B. z. A., lvi, 1903.

TUMOURS OF THE GLANDS OF THE LIDS

Milium is often seen upon the lids, and when multiple may be mistaken for xanthelasma. They are small, pearly-white, sebaceous tumours,

and are supposed to be retention cysts of sebaceous glands. They contain epithelial cells, which may be horny or fatty, and are rolled together into balls.

Sebaceous cysts occur here as elsewhere in the skin. The wall consists of connective tissue lined with flat cells, which show fatty and atheromatous changes. The contents are epithelial cells and fatty granules, and cholesterin is usually present.

Cysts of Moll's glands occur as small transparent cysts at the edge of the lid. They are retention cysts, and therefore allied to sudamina or miliaria.

The outer wall of the cysts consists of fibrous tissue, in which a few fine blood-vessels and striped muscle-fibres are embedded; it is therefore really the stretched superficial layer of integument, the papillæ being flattened out and lost, whilst any hair-follicles present are atrophic and extended over the convexity of the cyst. The inner wall consists of epithelium lying on a layer of unstriped muscle-fibres, which show that the cysts are derived from Moll's glands and not from ordinary sweat-glands, which do not possess this smooth musculature (Sattler[1]). The epithelium is of two kinds. In the *multilocular* cysts, which are derived from the gland tubules, the epithelium consists of short cubical cells in a single layer. In the *unilocular* cysts, which are derived from the gland ducts, there is a double or treble layer of epithelium consisting of flat cells with the long axes of the oval nuclei arranged horizontally, the cell walls being indistinguishable. Here the cells lie directly on the connective tissue, and there are no smooth muscle-fibres. The cysts contain a clear fluid, fairly rich in proteids. Under the microscope fine crystals are seen. Wedl and Bock found cholesterin crystals, Wintersteiner calcium sulphate; the latter is interesting in that sulphates are contained normally in sweat.

Proliferation of the walls of Moll's cysts may produce more or less solid tumours, which form a connecting link with the true adenomata. Wintersteiner has described a *cystadenoma papillare proliferum* of a Moll's gland from the vicinity of the lower punctum. The wall was covered by a single layer of flattened epithelium, which had proliferated in one part and formed a papillomatous projection into the cavity, thus very much resembling many ovarian cysts. This case appears to be unique in the literature.

Retention cysts of the Meibomian glands occur very rarely. In a case of Wintersteiner's the cyst was lined by flattened epithelium, mostly in a single layer, which lay upon dense thick fibrous tissue, the enormously stretched and thinned tarsus. The skin was extended over the anterior surface, the papillæ being flattened out and the muscles, etc., compressed and degenerated. The cyst contained fibrinous coagulum and granular *débris*. Such cysts have been produced artificially by Deyl by obliteration of the ducts through cicatrisation. This occurs frequently in the human subject in trachoma, and is by far the commonest cause of Meibomian cysts.

[1] SATTLER, Arch. f. mikr. Anat., xiii.

DESFOSSES.—A. d'O., i, 1881. WEDL AND BOCK.—Path. Anat. des Auges, Wien, 1886. WINTERSTEINER.—A. f. A., xxxiii, Ergänzungsheft, 1896; A. f. A., xl, 1899.

Adenomata have been described in connection with the sweat-glands Fuchs), sebaceous glands (Fuchs, Rumschewitsch), Moll's glands (Salzmann), Meibomian glands (Baldauf, Bock, Rumschewitsch,

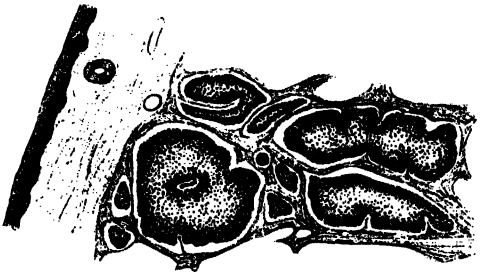


FIG. 12.—ADENOMA OF MEIBOMIAN GLAND. Reichert Obj. 2.
After Salzmann (A. f. A., xxii, Taf. iv), showing capsule, septa, and solid glandular cords, separated from the septa by lymph spaces.

Salzmann, Wadsworth, Knapp), Waldeyer's glands (Rumschewitsch), and Krause's glands (Moauro, Salzmann—*see* "Conjunctiva"). The exact origin of these tumours is seldom beyond dispute. A few others have been collected by Schirmer.

Meibomian adenomata (Figs. 12 and 13) are possibly commoner

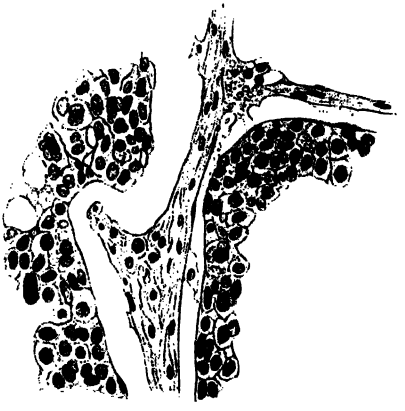


FIG. 13.—ADENOMA OF MEIBOMIAN GLAND. Reichert Obj. 8*a*.
After Salzmann. From the middle of the tumour, showing septa, with lymph spaces lined in places by endothelial cells, and the pathological gland-cells.

than the literature would lead one to expect. It is not unusual to meet with chalazia which are hard and do not respond to the usual treatment. It is possible that some of these are really adenomata. Those which

have been described consist of acini of very various sizes, mostly filled with cells, the peripheral ones being cylindrical, the central ones polygonal. There is rarely a small lumen. The peripheral cells show no fatty vacuoles, whilst the central ones are usually fatty and have no nuclei. The acini are separated by connective tissue containing blood-vessels, the adventitiæ of which are sometimes infiltrated with cells (Bock).

Adenomata of Moll's glands (Fig. 14) seem to tend much to cystic formation, which was present in Salzmann's case, and extreme in Wintersteiner's (*v.* p. 25). In Salzmann's case there was a large dendritic mass of tubular character, with a central cystic space. The cavity and tubules were lined with a double layer of cells—outer, low, cubical; inner, cylindrical. There were no smooth muscle-fibres around the tubules, as in the normal gland.

Adenomata of Krause's glands (Fig. 15) show branched and anasto-



FIG. 14.—ADENOMA OF MOLL'S GLAND. Reichert Obj. 4.
After Salzmann. From the periphery of the tumour, showing branched glandular tube, with regular double lining of epithelium.

mosing tubules lined with a single layer of cubical or cylindrical cells; in places a second layer of irregular cells lies on the inner surface. The lumen varies much in width, and often contains degenerated cells and granular *débris*. The stroma consists of loose connective tissue, sharply distinguished from the capsule of the tumour, which is formed out of the tarsal tissue.

FUCHS.—A. f. O., xxiv, 2, 1878. RUMSCHEWITSCH.—K. M. f. A., xxviii, 1890; xl, 1902. BALDAUF.—Inaug. Diss., München, 1876. BOCK.—Wiener klin. Woch., 1888. SCHIRMER.—A. f. O., xxxviii, 1, 1891. *SALZMANN.—A. f. A., xxii, 1891. MOAURO.—Riv. internaz. di Med. e Chir., iv, Napoli, 1887. WADSWORTH.—T. Am. O. S., 1895. *KNAPP.—T. Am. O. S., 1901.

Syringo-adenoma (Unna) is an excessively rare disease of the skin, which has been observed in the lids (Jarisch). It consists of cysts lined

by flat nucleated epithelium, and from these, duct-like cylinders of epithelial cells of about the thickness of a sweat-gland duct proceed. It is probably developed from "rests" of sweat-glands (Török), but the most various explanations have been brought forward.



FIG. 15.—ADENOMA OF KRAUSE'S GLAND. Reichert Obj. 8 *a*.

After Salzmann. The epithelium, double in places, is seen lying on the stroma, the lumen containing epithelial cells and *débris*. On the left, above, are epithelial processes cut longitudinally and transversely.

RADCLIFFE-CROCKER.—Diseases of the Skin, London, 1903.

Carcinoma of the Meibomian glands has been reported and figured by Panas. Some of the acini were normal, whilst others were filled with cells of epitheliomatous type, some forming concentric nests with mucoid degeneration in the centre. Other cells contained inclusions resembling coccidia.

Fuchs has described a carcinoma of the Meibomian or of Krause's glands which invaded the tarsus, the latter showing hyaline degeneration.

Cases are also reported by Snell, and Scott and Griffith. The latter was a typical alveolar carcinoma, the cells showing great diversity of character. Some were exactly like sebaceous epithelium, and in some sections of the Meibomian glands the cells had perforated the basement membrane and were invading the tarsus.

An *adeno-carcinoma* of the Meibomian glands has been published by v. Grosz, and a similar one by Snell.

It is possible that carcinoma occasionally starts in other glands of the skin and lids. Some rodent ulcers show a glandular type of carcinoma in places (*v.* p. 24).

PANAS.—Traité des Maladies des Yeux, ii, Paris, 1894. FUCHS.—A. f. O., xxiv, 2, 1878. v. GROSZ.—C. f. A., xx, 1896. SNELL.—T. O. S., xvi, 1896. SCOTT AND GRIFFITH. —T. O. S., xx, 1900.

CONGENITAL TUMOURS

Congenital tumours are nævi and dermoids.

Nævi, or moles, usually pigmented, have exactly the same structure histologically as those of the conjunctiva, and are fully dealt with under that heading.

Dermoid cysts are really orbital tumours which press forward the lid, and will be considered under "Tumours of the Orbit."

Solid **dermoids** also occur, and cases described as supernumerary caruncle probably belong to this group (Eyre, Stephenson). In Eyre's case the tumour occupied the space between the upper punctum lacrymale and the inner canthus. It was covered by stratified epithelium, and contained hair-follicles, sebaceous and mucous glands, and striped and smooth muscle.

EYRE.—A. of O., xxvi, 1897; T. O. S., xviii, 1898. STEPHENSON.—Ophth. Rev., xv, 1896.

CHAPTER II

THE CONJUNCTIVA

THE NORMAL CONJUNCTIVA

THE conjunctiva is a mucous membrane covering the margin and posterior surface of the lids, and reflected on to the globe. In the cornea it is represented by the epithelium, so that it may be regarded as a sac, open only in front at the palpebral aperture.

It is divided anatomically into three parts: (1) the C. palpebrarum, subdivided into a marginal part, a tarsal part (C. tarsi), and an orbital part; (2) the fornix, or C. fornicis; (3) the C. bulbi. Histologically it consists of two layers: (1) the epithelium; (2) the substantia propria.

The *epithelium* varies in different parts of the conjunctiva and at different ages. It is only found typically developed in the new-born infant. This is accounted for by the fact that the irritating effects of dust, etc., soon leave their mark and are ineradicable. There is, however, a fundamental difference in different parts, and this manifests itself in the specific character of various pathological conditions, and in their punctilious limitation to definite areas.

The intermarginal zone of the lid between the anterior and posterior borders (*v.* p. 2) is covered with stratified epithelium, and this passes upwards for a short distance on to the posterior surface of the lid. This part of the lid is in closest apposition with the globe, and mutual pressure of the two may perhaps be the cause of the flattening of the superficial cells. It ceases in a line parallel with the posterior border of the lid, which shows a slight depression and is called the *sulcus subtarsalis*. The cells of the middle layers of the intermarginal zone are prickle-cells, so that the epithelium resembles epidermis histologically rather than mucous membrane. There is therefore little more reason for calling this conjunctiva than skin. It is a true transition zone.

The C. palpebrarum is covered with two layers of epithelium—a superficial cylindrical, and a deep flattened. The superficial cells are tall, cylindrical or pyramidal, with oval nuclei, the long axes of which

coincide with those of the cells. The nucleus usually lies near the base of the cell; it stains faintly with hæmatoxylin. The cytoplasm is copious and finely granular. The cells are united by a minimum of cement substance, which stains with silver nitrate. The bases of the cells are often separated by minute spaces. The deep cells are flat, with oval nuclei, directed horizontally and staining deeply. This double layer of cells is only found on the C. tarsi, and even here intercalated cells are not uncommon, leading to a triple lamination. This tendency increases in the orbital part and fornix, and reaches its maximum at the limbus, where the epithelium is definitely stratified. In this manner a middle layer is gradually formed. The cells of which it is formed most resemble the deeper cells, but are larger, polygonal by mutual pressure, separated only by cement substance, and provided with centrally situated round or oval nuclei. As the limbus is approached the basal cells become more cubical, and finally cylindrical, whilst the superficial cells become flatter. At the limbus the superficial layer consists of one or two layers of flat cells with well-marked horizontal oval nuclei; the middle layer of many layers of polygonal cells, which are distinguished from the adjacent corneal cells by the absence of prickles, cement substance alone uniting them; the basal layer of a single layer of small cylindrical or cubical cells, with large, darkly staining nuclei and little cytoplasm, often containing pigment granules. True papillæ are found at the limbus (Ciaccio, Nakagawa), *i. e.* finger-like extrusions of the substantia propria, the interspaces of which are filled with epithelium, whilst the surface of the epithelium remains flat. There are usually only four or five large papillæ (50 μ high) near the cornea, and three or four smaller ones (13—32 μ high) more peripherally (Villard).

Goblet-cells are found normally in the epithelium of the whole conjunctiva, but especially in that of the C. bulbi and fornix (Fig. 16). They much resemble the goblet-cells of the intestine, but show interesting peculiarities. In the fresh state they are large round or oval cells, strongly refractile, and much like fat-cells. They are found at various depths, the deeper ones being smaller and round, the superficial ones oval and larger than the epithelial cells (25 μ by 16 μ [Green]), and possessing a definite opening or stoma upon the surface. They have a double-contoured membrane or theca (Green), and a pointed process below, which often reaches down to the basement membrane (Peters). The main contents of the cell consist of mucin, which forms homogeneous or finely granular droplets when fresh, and larger granules or networks when hardened. This secretion pushes aside the cytoplasm, which is almost invisible, and the flattened nucleus forms a crescent at the base. The latter may be apparently absent in thin sections owing to the size of the cells. Only the superficial cells have a stoma, and the mucin is often seen protruding from it. The stomata are well displayed in surface preparations when the outlines of the neighbouring cells are marked out by silver staining (Greeff). The secretion stains very variously. It is more or less extracted during the process of hardening, unless fixed by acetic acid, and even then stains variously, owing probably to the presence of intermediate products (mucinogen). The

fresh mucin usually stains with hæmatoxylin and basic aniline dyes—best with thionin. The superficial cells give the best thionin reaction, owing to the greater quantity of the final product (mucin) present.

Leydig (1857) first discovered such cells in the epidermis of the fish, and called them "mucous cells" (Schleimzellen). They were called "goblet-cells" (Becherzellen) by Schulze (1863), as it was doubtful if they all contained mucin. Stieda (1867) first found them in the conjunctiva, and called them "unicellular mucous glands." Waldeyer (1874) adopted this idea, pointing out the tendency of the cylinder-cells to become metamorphosed into goblet-cells. Now these cells are found in far greater numbers in conditions of chronic inflammation, so that Sattler (1877) looked upon them as pathological. They are also more numerous in tumours (papillomata, etc.). Since, however, they



FIG. 16.—GOBLET-CELLS IN THE CONJUNCTIVA. × 120.

Goblet-cells, with the nuclei pressed down to the base, are seen in all the layers of the epithelium. Below is slight lymphocytic infiltration, evidence of chronic irritation. There is also a dilated lymphatic space filled with hyaline material.

occur in the fœtus and new-born, and were found by Green in thirty consecutive normal conjunctivæ, they may be regarded as normal, though subject to great and even enormous increase under pathological conditions. Stieda, in 1890, altered his previous opinion that they were secretory cells, and regarded them as degenerated cells. It seems probable, indeed, that the cells are destroyed after they have expelled their contents, secretory activity ending in destruction; and in this respect they may be compared with the cells of the active mammary gland. Though resembling the goblet-cells of the intestine, they are not identical with them. The latter are formed only upon the surface, and regenerate after expelling their contents. The former are much more nearly allied to the epiblastic cells described by Leydig in fishes and the larvæ of amphibia (Pfitzner). They are apparently formed

only from the cylindrical cells, *i. e.* mostly from the deepest layer, remain closed as they pass towards the surface, still retaining a filamentary connection with the basement membrane, and finally open upon the surface, expelling their contents, thereby being destroyed. Their function can hardly be considered doubtful. They are true unicellular mucous glands, moistening and protecting the conjunctiva and cornea, so that even extirpation of the lacrymal gland is innocuous; whilst, on the other hand, xerosis of the conjunctiva, involving their destruction, leads to desiccation in spite of a copious flow of tears (Greeff).

We have seen that true papillæ, in which the surface epithelium remains level, only occur near the limbus. Papillæ are described in other parts in pathological conditions; they are not true papillæ, however, but undulations produced by swellings in the substantia propria. Similarly depressions in the surface have been described as glands. The conjunctival surface is only smooth in new-born infants (Stieda, Sattler, Raehlmann, etc.), *i. e.* before the adenoid tissue is developed in

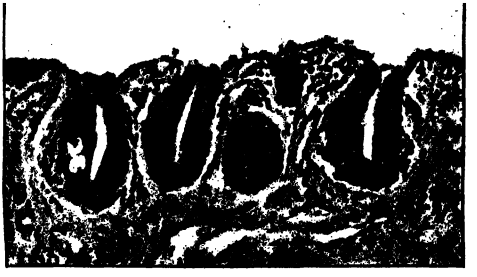


FIG. 17.—HENLE'S GLANDS.
From a photograph by Lister.

the substantia propria. C. Krause (1842), Gerlach (1852), and Kölliker (1863), in their text-books of anatomy, described the papillary nature of the conjunctiva, and even the presence of small mucous glands (Krause). Henle (1866), in his text-book, regarded the tops of the "papillæ" as the normal level, and described the depressions as glands, which have since been known as *Henle's glands* (Fig. 17). They consist of depressions in the basement membrane, some vertical, others oblique, of various length, lined by regular cylindrical epithelium. Stieda first cut sections parallel to the surface, and found that the so-called glands were not regular tubular depressions, but folds and furrows (Stieda's 'Rinnen und Falten-system'), having round or irregular contours of various sizes. In sections in other directions these are cut across so as to produce the most various appearances, much resembling true glandular structures. They are naturally most marked in the central parts of the upper fold, especially near the upper part of the tarsus, gradually fading off towards the canthi. The cylindrical shape of the cells is characteristic of all depressions, where the epithelium is less exposed to pressure. True tubular glands are normally present

just beyond the limbus in the calf and ox (Meissner), and in the pig (Manz). The presence of tubular glands in the C. tarsi is doubtful. Tubular depressions, however, do occur, which cannot be fully explained by folds (Stieda, Jacobson, Sattler), especially in the nasal parts of the lid (*Baumgarten's tubular glands*).

True large acino-tubular glands (*Krause's glands, accessory lacrymal glands*) occur below the surface between the fornix and the edge of the tarsus, especially towards the nasal side. There are about forty-two in the upper, and six to eight in the lower fornix (W. Krause). They are serous glands, exactly resembling the lacrymal gland, and, indeed, forming offshoots of the inferior lacrymal gland. The ducts of numerous acini unite to form a larger duct which opens on to the fornix.

The *substantia propria* consists of adenoid connective tissue. The reticulum of fibrous tissue contains many lymphocytes in its meshes, especially in the superficial layers, so that a division is sometimes made into a superficial adenoid layer and a deep fibrous layer. The adenoid layer is absent in the new-born, and commences two or three months after birth by the invasion of the fibrillary tissue at certain spots in the fornix (Raehlmann). It is the development of this layer, accompanied by increase in the superficial area, which leads at about the end of the fifth month to the formation of folds in the upper third of the C. palpebrarum (Raehlmann).

The adenoid layer is thin, but varies—40 μ in the C. palpebrarum, 50—70 μ in the fornix, 15—27 μ in the C. bulbi (Villard). It ceases at the sulcus subtarsalis, and is therefore absent under the stratified epithelium from that line to the anterior border of the lid. The meshes consist of extremely fine fibres. The lymphocytes are usually numerous in all parts, even in quite normal conjunctivæ, but are enormously increased in conjunctivitis. They are usually distributed regularly, but much discussion has arisen as to whether *follicles* normally occur (*see* "Trachoma"). They are constant, especially near the lower fornix, in many animals (dog, cat, rabbit, etc.). Nodules of lymphocytes are frequently found in the human conjunctiva, but they usually fade off at the periphery, and do not form true follicles. The pathological development of these follicles leads to undulations in the surface—pseudo-papillæ.

The fibrous layer is thicker than the adenoid, and composed of thicker meshes, which contain many elastic fibres. The density of this layer offers great obstacles to cellular infiltration. The layer is thin over the tarsus, with which it is continuous. In other parts it is looser. The posterior insertion of the levator palpebræ fades off into it at the fornix, which is thus lifted up in upward movements of the lid.

The chief arteries, veins, lymphatics, and nerves lie in the fibrous layer, but the adenoid layer is very richly supplied.

The *plica semilunaris* is a simple fold of the C. bulbi near the inner canthus. It is the vestige of the nictitating membrane, and as such sometimes contains a small cartilaginous plate (Buschmann, Eversbusch) and an acinous gland (Giacomini), the remnant of the *Harderian*

gland. It has been found enlarged on one or both sides in a few cases, resembling the true nictitating membrane (Herzenstein, Eversbusch), or hypertrophied into a tumour (Rumschewitsch). It is doubtful if these were true hypertrophies.

The *caruncle* is an outlying patch of skin, the epithelium of which has become modified by environment, having two layers like the C. tarsi, increased by several middle layers on the summit. Goblet-cells, glandular depressions, and fine hairs with sebaceous glands are always present. Glands resembling Krause's glands are present (Krause, Giacomini, etc.), and, according to some authors, sweat-glands (Waldeyer, Sattler, Rumschewitsch). There are fat globules in the corium.

CIACCIO.—Mém. de l'Acad. des Sc. de l'Institut de Bologne, 1873. NAKAGAWA.—A. f. A., xlvii, 1903. VILLARD.—Anat. path. de la Conjonctive granuleuse, Paris, 1896. *GREEN.—A. f. O., xl, 1, 1894. PETERS.—C. f. A., xxi, 1897. STIEDA.—Arch. f. mikr. Anat., iii, 1867. WALDEYER.—In G.-S., i, 1874. REICH.—A. f. O., xxi, 1, 1875. SATTLER.—A. f. O., xxiii, 4, 1877. WOLFRING.—K. M. f. A., 1878, Beilageheft. JACOBSON.—A. f. O., xxv, 2, 1879. BAUMGARTEN.—A. f. O., xxvi, 1, 1880. RAEHLMANN.—A. f. O., xxix, 2, 1883. WALDEYER.—In de Wecker and Landolt, Traité, ii, Paris, 1886 (Bibliography). STIEDA.—Arch. f. mikr. Anat., xxxvi, 1890. TERSON.—A. d'O., xii, 1892. PFITZNER.—Zeitschrift f. Biologie, xxxiv, 1896. *GREEFF.—In Orth, Lehrbuch d. spec. path. Anat., 1902. BUSCHMANN.—Arch. ital. de Biol., ix, 1887. GIACOMINI.—Annotazioni sopra l'Anat. del Negro, Torino, 1878. HERZENSTEIN.—Centralbl. f. d. med. Wissensch., 1879. EVERSBUSCH.—Festschrift des Münch. Aerztevereins, 1883. RUMSCHEWITSCH.—K. M. f. A., xl, 1902; xli, 1903.

THE BACTERIOLOGY OF THE CONJUNCTIVA

THE NORMAL CONJUNCTIVA

The normal conjunctiva in the new-born is free from bacteria. Koblank investigated this point in twenty cases by culture experiments, which were negative. He attributes it to the fact that the lids remain closed *intra-partum.* Cramer proved that they may open. In some cases xerosis bacilli and staphylococci were found on the second day; in others the conjunctiva was still sterile on the sixth day. In any case the bacteria are few during the first ten days.

WALTHARD.—In Pflüger, Korrespondenzbl. f. Schweizer Aerzte, 1895. KOBLANK.—Festschrift f. Karl Ruge, Berlin, 1898. CRAMER.—Centralbl. f. Gynäkologie, No. 9, 1899.

The conjunctival sac is open to the air, and is in intimate proximity to the skin. It is not surprising, therefore, that it should contain many bacteria from both of these sources. It is more surprising that so large a proportion of sterile conjunctivæ should have been found by various authors (Foote, 50 per cent. in children, 33 per cent. in young people, 30 per cent. in old people; Eyre, 50 per cent.). Still, there can be no doubt that the number of organisms varies greatly (Eyre), whilst their nature and pathogenicity, and the possibility of sterilisation, are subjects of much dispute. The xerosis bacillus is most commonly found (Heinersdorff, Lawson, Axenfeld [1], Gifford), and after that the

Staphylococcus albus. Lawson alone found the latter seldom (6 out of 200 cases). Gasparrini found the pneumococcus in 80 per cent. of cases, which has been shown to be a mistake by Oertzen (4 per cent.). Lawson found it twice in 200 cases. According to my own experience small diplococci are not uncommon in the conjunctiva, and they probably include many species, some of which have been mistaken for pneumococci.

The staphylococci found are usually of slight virulence. Virulent pyogenic staphylococci (*aureus* and *albus*), streptococci, etc., are rare.

The identity of the xerosis bacillus will be discussed later.

Other pathogenic and non-pathogenic bacteria are found occasionally. In this connection it need only be noted that Lobanow found that amongst the non-pathogenic organisms the *Sarcina lutea*, *Proteus*, *B. subtilis*, *prodigiosus*, *agilis*, *fluorescens*, *putridus*, and *Micrococcus roseus*, introduced into the anterior chamber and vitreous of the rabbit, produced a slight, non-progressive inflammation.

Bach investigated the influence of movements of the lids and of tears upon the bacteria. He showed that within twenty-four hours organisms (Kiel water bacillus, *Staph. pyog. aureus*) were transported from the conjunctiva to the nose. Transference from the nose to the conjunctiva could never be obtained with normal flow of tears (this was confirmed by Hauenschild). He confirmed Bernheim's dictum that the tears were slightly bactericidal; this is probably not due to serum-albumen (Bernheim), but to mere dilution, just as with salt solution, water, etc. (Morax, Bach). de Bono and Frisco inoculated the tears of goats, asses, and calves with *Staph. pyog. aureus*, diphtheria bacillus, etc., and inoculated culture media from them after ½, 1, 4, 14, 48 hours. After 48 hours the number of bacteria was definitely increased, though a slight diminution took place in the first hour. The toxicity of tubercle bacilli was not diminished; that of diphtheria bacilli was remarkably so—inoculation with freshly infected tears killed in seven days (control in two days); after six hours the inoculated animals did not die. Whether these experiments can be regarded as true for man is doubtful; the Harderian secretion must be taken into account. Axenfeld (2) concludes that the bactericidal property of tears is as yet by no means definitely proved. The tears are doubtless a bad culture medium; many bacteria must die, but a definite bactericidal property is questionable.

The possibility of sterilising the conjunctiva is a question of grave practical importance. Bach showed that mechanical purification of the lids, combined with irrigation of the conjunctiva with saline solution, led to great diminution in the micro-organisms, amounting to sterilisation in nearly half the cases. There was no greater effect with antiseptics, but it must be noted that perchloride of mercury (1 in 2000) was used for the lids. Morax, however, found no difference. The importance of non-irritative lotions is emphasised by many authors. Widmark found microscopic changes in the epithelium with sublimate solutions of 1 in 5000, and even 1 in 10,000. It is generally admitted that complete sterilisation is in most cases unattainable (Bach [2] for formol, 1 in 2000 or 3000; Franke for sublimate, 1 in 5000; Gifford,

McGillivray), even though it be occasionally attained. Franke disagrees with Bach and Morax in that he obtained better results with sublimate than with saline irrigation. Much doubtless depends upon mere mechanical details. Hauenschild published statistics of the Würzburg clinic from 1893 to 1898—1944 operations upon the globe, including 549 cataracts—with asepsis only, and only one suppuration.

Nearly allied is the question of the influence of bandaging upon the number of micro-organisms found. Odhelius (1772—1807) is said to have recommended the open treatment of wounds, and bandages were occasionally dispensed with by Demours and Desmarres (Rohmer). It has been used in an unqualified manner by Hjort. Clarke has published experiments tending to show that the anterior chamber is most rapidly refilled in corneal wounds in rabbits when the animals are kept at rest by an anæsthetic (five to fifteen minutes), whereas, if they are allowed to recover, the movements of the animal so interfere with the process that it is not complete for two hours. This tendency to a delayed adhesion of the lips of the wound, being in favour of infection, must be set against any tendency of the lid movements, by increasing the current of tears, to diminish the bacteria in the conjunctival sac. And, indeed, the evidence in favour of the latter tendency is by no means conclusive. Daléns found that after five to eight hours' bandaging the bacteria were decidedly fewer than before disinfection (twenty experiments in ten people), whilst after twelve to fourteen hours' bandaging (forty experiments in twenty people) a variable result was obtained—increase in both eyes in four, diminution in both eyes in seven, and increase in one eye with diminution in the other in six. The indications of these experiments seem to be in favour of bandaging until the wound is closed, after which movements of the lids are not harmful, and may even be beneficial.

FICK.—U. die Mikroorganismen im Konjunktivalsak, Wiesbaden, 1887. FOOTE.—Med. Record, 1896. EYRE.—Annals of Ophth., 1897. HEINERSDORFF.—A. f. O., xlvi, 1, 1898. LAWSON.—Brit. Med. Jl., 1898. AXENFELD (1).—Berlin. klin. Woch., 1898. GIFFORD.—A. f. A., xxxix, 1899. GASPARRINI.—Ann. di Ott., xxii, 6, 1894. OERTZEN.—K. M. f. A., xxxviii, 1899. LOBANOW.—In *Lubarsch and Ostertag, Ergebnisse der allg. Path., Wiesbaden, 1901. BACH (1).—A. f. O., xl, 3, 1894. DE BONO AND FRISCO.—Arch. di Ott., vii, 1899. *AXENFELD (2).—In Lubarsch and Ostertag, Wiesbaden, 1901. MORAX.—Thèse de Paris, 1894. BAÇH (2).—A. f. A., xxxv, 1897. FRANKE.—A. f. O., xliii, 1, 1897. MCGILLIVRAY.—Ophth. Rev., xvii, 1898. HAUENSCHILD.—Z. f. A., ii, 1899. ROHMER.—Ann. d'Oc., cxxi, 1899. HJORT.—C. f. A., xxi, 1897; xxii, 1898. CLARKE.—T. O. S., xviii, 1898. DALÉNS.—In Lubarsch and Ostertag, Wiesbaden, 1901. GRIFFITH.—Thompson-Yates Lab. Rep., iv, 1901.

CONJUNCTIVITIS

The present state of knowledge unfortunately does not admit of an accurate classification of the various forms of conjunctivitis upon a pathological basis. In only very few cases is it possible to specify a definite micro-organism as the *causa causans* of a given clinical type of inflammation. Nor is this surprising when we consider the multitudinous factors at work. The interaction and reaction of organism and tissue, with the modifying influences of toxicity and immunity—relative or absolute,—cannot be too often or too forcibly insisted upon.

The pathologist too readily imagines that his experiments *in vitro* will be unchanged *in corpore vili*, whilst the clinician expects all his difficulties to be solved by a film or a culture-tube. When we add to these distracting factors the phenomena of mixed infections, the bewildering complexity of the subject is complete.

It is therefore necessary to treat the bacteriology of conjunctivitis apart from the clinical types, and incidentally to collate the two, and as far as is possible show their true relationships. A valuable brief *résumé* will be found in a paper by Uhthoff (1898), and most of the recent literature in Lubarsch and Ostertag.

*Uhthoff.—Vossius' Sammlung, ii, 5, 1898. *Lubarsch and Ostertag.—Ergebnisse der allgemeinen Path. u. path. Anat. des Auges., Wiesbaden, 1894, 1895-6, 1897-8-9. *Axenfeld.—In Kolle and Wassermann, Handbuch der path. Microorganismen, Jena, 1903.

Staphylococci

Staphylococci are constantly found in the skin at the edge of the lids, and, as we have seen, they often find their way into the normal conjunctival sac. *St. albus* in a non-virulent form is common; *St. aureus* is rarer. They have been wrongly regarded as the cause of phlyctenular conjunctivitis by many authors (q. v.). Whether they are of ætiological moment in the cases of ophthalmia neonatorum (q. v.) and membranous conjunctivitis (q. v.), in which they occur in large numbers, is uncertain. It is doubtful whether an endogenous staphylococcic conjunctivitis exists, as has been described in measles (Barbier, Cuénod) and other exanthemata. Staphylococci have been most often described in cases of pseudo-membranous conjunctivitis (Gasparrini, Valude, Pichler, Bietti, etc.). In man, all experiments for producing conjunctivitis by rubbing virulent *S. aureus* cultures into the intact conjunctival sac have hitherto failed.

Valude.—Ann. d'Oc., cxi, 1894. Pichler.—B. z. A., xxiv, 1896. Bietti.—Ann. di Ott., xxvi, 1897; K. M. f. A., xli, Beilageheft, 1903.

Streptococci

Streptococci never occur in the normal conjunctiva according to most authors (Fick, Marthen, Morax, etc.); relatively frequently according to Gasparrini, Villeneuve, etc.; rarely according to Uhthoff. Streptococcic conjunctivitis occurs in two chief groups, a simple catarrhal and a pseudo-membranous form.

The simple catarrhal form is known as *Parinaud's lacrymal conjunctivitis*. It is a rare condition, associated with dacryocystitis; it is often unilateral. The conjunctiva, especially the bulbar conjunctiva, is intensely injected and moderately thickened; there is slight secretion, and some swelling of the lids. Iritis is relatively frequent, especially as "serous" iritis; the preauricular and cervical glands are often swollen and painful, and there is a general febrile condition. Several of the cases occurred in butchers, or people employed with cattle, so that Parinaud attributed the disease to an animal origin. The subject has

been investigated by Gasparrini, Valude, Bardelli, Axenfeld, Gifford, etc. Most observers found streptococci, but their ætiological significance cannot be said to be proved beyond cavil. Morax found the aqueous sterile in one case, so that the irido-cyclitis is probably due to the absorption of toxins; indeed, Bardelli succeeded in producing kerato-iritis in rabbits by repeated irrigation of the conjunctival sac with dead, filtered bouillon cultures.

The pseudo-membranous form is met with more frequently; Coppez has collected thirteen cases from the literature, and Uhthoff has seen several. They often ended with loss of the eye through ulceration of the cornea, and occasionally in death of the patient. Cases of mixed streptococcic and diphtherial infection are reported (Franke). Streptococci may be present in large numbers in impetigo of the face, and the association of this condition with membranous conjunctivitis is well established (Uhthoff).

Occasionally endogenous streptococcic conjunctivitis occurs, accompanied by great swelling of the lids and moderate secretion. Leber and Wagenmann, and Axenfeld report two such cases, both in new-born children, ending fatally: in the first there was partial necrosis of the conjunctiva; the second resembled ophthalmia neonatorum. In both there were streptococcic thrombi in the conjunctival vessels. In Leber and Wagenmann's case death followed the day after onset of the conjunctivitis, so that it could scarcely be the primary seat of infection.

MARTHEN.—B. z. A., xii, 1895. VILLENEUVE.—Thèse de Paris, 1896. PARINAUD.—Ann. d'Oc., cvii, 1892. BARDELLI.—Ann. di Ott., xiv, 1895. AXENFELD.—Münch. med. Woch., 1898. GIFFORD.—Amer. Jl. of Ophth., xv, 1898. COPPEZ.—Des Conjonctivites pseudomembraneuses, Paris et Bruxelles, 1897. FRANKE.—Münch. med. Woch., 1883. LEBER AND WAGENMANN.—A. f. O., xxxiv, 4, 1888. AXENFELD.—A. f. O., xl, 3 and 4, 1894.

THE PNEUMOCOCCUS (FRÄNKEL—WEICHSELBAUM)

The *Diplococcus lanceolatus* or pneumococcus occurs rarely in the normal conjunctiva. It has been the cause of severe epidemics, both in Europe and America, the organism being rare only in Egypt. It is commonest in children, and was first described by Parinaud and Morax in the new-born. It had been previously described in hypopyon ulcers by Gasparrini, who showed that it produced conjunctivitis in rabbits; it is indeed the cause of the typical hypopyon ulcer—ulcus serpens (Uhthoff and Axenfeld). Axenfeld investigated an epidemic at Marburg, and confirmed its predilection for young children. Gifford, however, in an epidemic in Omaha, found about half the cases in adults. Junius found thirty-six out of forty-nine patients young. Gifford was able to cultivate the organism, and reproduce the disease in men from the cultures; but pneumococcic conjunctivitis is not invariably contagious, predisposition on the part of the patient being necessary. There is slight rose-red œdema at first, followed by great swelling, and occasional formation of a membrane (Morax, Axenfeld, Coppez, Pichler). The secretion is watery, and small hæmorrhages are common, especially in the upper lid (Axenfeld, Uhthoff, Junius). Gifford saw greater varia-

tion in the cases. Cases also occur sporadically. Infection of the cornea is rare, since the toxin has no effect upon the intact epithelium (Coppez). Follicles are only formed rarely, and rapidly disappear (Axenfeld, Junius). There is an incubation period of forty-eight hours (Gifford).

E. v. Hippel found pneumococci which were not virulent to rabbits in a case of congenital purulent conjunctivitis, *i. e.* pus was present in the conjunctival sac at birth.

The pneumococcus is very wide-spread both geographically and pathologically. It was discovered independently in human saliva in 1880–81 by Sternberg and Pasteur. It was shown by Fränkel, confirmed by Weichselbaum, to be the cause of lobar pneumonia, but it also occurs in otitis media, purulent meningitis, etc. The appearance



FIG. 18.—PNEUMOCOCCI. × 1000.

Specimen by Mayou, taken from conjunctival sac; photograph by Henderson. Cultures were taken the day after development of a minute corneal ulcer; they were virulent for mice.

in cover-glass preparations is often characteristic; at other times it must be substantiated by cultures, and always when possible by inoculations. Stained with methylene blue, the diplococci have a typical lanceolate shape, and are surrounded by a faintly stained capsule (Fig. 18), which may, however, be absent in conjunctival forms. They often form short chains of four to six or even more members. There are other characteristics which tend to show that it belongs to the *Streptococcus pyogenes* group. If so, it is specially differentiated, as is further shown by the difficulty of cultivating it, mucous secretions being its normal habitat. It is stained by Gram's method, but the capsule is then decolourised. The meningococcus is decolourised by Gram. The pneumococcus grows best on alkaline media at 35° C.,

forming transparent round colonies. Films from the cultures show no capsules. The virulence is soon lost on agar or blood-serum, but is retained longer in bouillon. Inoculations of the fresh bouillon cultures into guinea-pigs, mice or rabbits leads to death in twenty-four hours from septicæmia, with characteristic œdema and swelling of the spleen. Inoculation of a white mouse with cultures is not invariably lethal even in typical cases of conjunctivitis (Uhthoff).

PARINAUD.—Ann. d'Oc., cxii, 1894. MORAX.—Thèse de Paris, 1894. GASPARRINI.—Ann. di Ott., xxii, 1893; xxiii, 1894; xxv, 1896. UHTHOFF AND AXENFELD.—Berl. klin. Woch., 1895; A. f. O., xlii, 1, 1896. AXENFELD.—Münch. med. Woch., 1898. GIFFORD.—A. of O., xxv, 1896. JUNIUS.—Z. f. A., i, 1899. OERTZEN.—K. M. f. A., xxxvii, 1899. GONIN.—Rev. méd. de la Suisse Romande, 1899. VEASEY.—A. of O., xxviii, 1899. VEASEY AND DE SCHWEINITZ.—Ophth. Rev., xviii, 1899. KIBBE.—A. f. A., xxxviii, 1899. COPPEZ.—Z. f. A., ii, Beilageheft, 1899. E. v. HIPPEL.—A. f. O., xlvii, 1, 1898. PETIT.—Ann. d'Oc., cxxvi, 1901. HAUENSCHILD.—Z. f. A., iii, 1900. DENIG.—Z. f. A., iii, 1900. HERTEL.—A. f. O., liii, 3, 1902.

THE GONOCOCCUS (NEISSER)

Gonorrhœal conjunctivitis occurs most commonly in new-born children as a severe type of ophthalmia neonatorum, and in young adults. It also occurs as a metastatic infection. It is characterised by an intense chemosis, with marked papillary development, and profuse purulent discharge. It is always acute, never becoming chronic, but ending in resolution, most frequently after partial or complete destruction of the eye. In the later stages there is a marked tendency to form a membrane (Streatfield, etc.). This may also occur in the early stages (Uhthoff). Follicles are never formed, and scars are not usually left in the conjunctiva. In these respects it differs essentially from trachoma, though, of course, each may be present independently. The gonococcus is unique in its ability to invade the normal corneal epithelium, especially when the pus is allowed to stagnate. This is followed by ulceration of the cornea, and the dangers of panophthalmitis.

The gonococcus is invariably contagious, but it is remarkable that the proportion of persons suffering from gonorrhœa who have gonorrhœal ophthalmia is so small. This is doubtless due chiefly to the protection which the lids and tears afford, but it is possibly also due in part to a low degree of immunity conferred by the disease. Evidence, however, on this point is lacking.

Endogenous gonorrhœal conjunctivitis (Haltenhoff), and especially iritis (Cheatham, Griffith, Lawford), is now proved. It has long been considered probable (Brandes, 1854; Fournier, 1866). Just as gonococci can be carried in the blood-stream to the joints, and there set up inflammation, the same may happen to the eyes. In fact, it is most commonly found in those cases in which the joints are affected. As in the joints, so in the eyes, gonococci themselves are generally absent; they are probably present in the tissues, but not in the secretions; but the possibility of a general toxæmia, manifesting itself in weak spots, must not be overlooked. Morax found gonococci in the conjunctiva in two cases. It is also characteristic of these metastatic gonorrhœal

affections that the urethral lesion is generally a mixed infection, the periurethral tissues containing staphylococci and streptococci in addition to gonococci (Loeb, Koenig, Neisser and Bumm). The conjunctivitis often recurs, not necessarily simultaneously with the joint affection (Gielen). Metastatic retinitis and optic neuritis have also been described.

Metastasis from a primary gonorrhœal conjunctivitis is much rarer, but cases have been proved. They occur mostly in new-born children, the joints being usually affected. Deutschmann and Clement Lucas found gonococci in the pus from the knee in some cases. The rarity is probably due to the free exit of discharge from the conjunctiva as compared with the urethra (Clement Lucas). The literature will be found in Altland's paper.

A rare type of infection is intra-uterine, either by endogenous

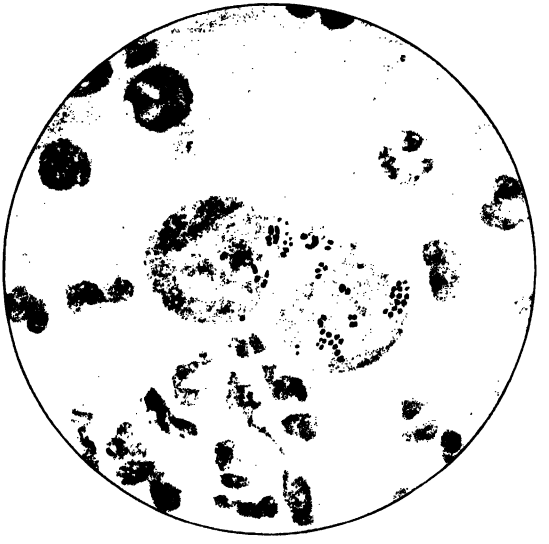


FIG. 19.—GONOCOCCI. × 1000.

Specimen by McNab, taken from conjunctival sac, stained with Unna's pyronin-methyl green mixture. Photograph by Henderson.

metastasis by the blood-channels, or by infection from the vagina, or introduced *per vaginam* (*cf.* E. v. Hippel). Thus, as regards endogenous transmission, it is known that anthrax, glanders, tubercle, typhus, pneumococcus, streptococcus, and *Staphylococcus aureus* can be transmitted to the fœtus. Panas ascribes a case of congenital phthisis bulbi to variola in the mother (*see* Leber and Addario). Intra-uterine infection by gonococci has been found by Parischeff in a case in which the membranes ruptured three days before birth, and by Nieden in a case in which the fœtus was expelled in the intact membranes. These cases are not wholly free from the possibility of post-partum infection.

Purulent conjunctivitis is by no means always caused by gonococci. In forty-two cases Gonin found them twenty-eight times, Koch-Weeks

bacillus eight times, staphylococci once, streptococci once. This agrees with our experience at Moorfields.

Similarly ophthalmia neonatorum can only in part be referred to the gonococcus; it is absent in a considerable proportion of cases, and other organisms are found (diplococci, pneumococci, streptococci, *Bacterium coli*, etc.). Both simple catarrh and blennorrhœa can be caused by these different organisms in the new-born; bad blennorrhœa may show no gonococci, and exceptionally slight catarrh may be caused by them; gonococcic blennorrhœa has a severe course and longer duration; ulcers occur both in the blennorrhœic and in the slight cases; gonococci are to be found in the conjunctival sac for days and even weeks after the cessation of purulent discharge—hence the need of protracted treatment (Groenouw). In a great number of cases, especially of slight conjunctivitis in the new-born, no specific organisms can be found. It is interesting to note that streptococci, gonococci, and *Bacterium coli* are amongst the common organisms found in the genital tracts of puerperal women (Menge and Kroenig). These authors did not find pneumococci, but they must occasionally be present, since they are sometimes the cause of puerperal fever.

The *Diplococcus gonorrhœæ* is a bun-shaped diplococcus, discovered by Neisser in 1879 (Fig. 19). It is readily stained by methylene blue, and resembles the meningococcus both morphologically and in the fact that it is decolourised by Gram's method. In this respect both differ from the pneumococcus. Nothing is known of its capacity to exist under saprophytic conditions, but it is almost an obligate parasite, and that, too, of man alone, for it is not found in other animals.

Besides its characteristic shape and its decolorisation by Gram, it is peculiar in being found in unusually large numbers within the cytoplasm of polymorphonuclear leucocytes. Here they are grouped in pairs or heaps around the nuclei of the cells. These features suffice in all cases to distinguish the gonococcus from staphylococci, streptococci, pneumococci, and most other micrococci; and this is fortunate, since the organism is cultivated with considerable difficulty. It grows best at 32°—34° upon human blood-serum, or a mixture of agar with ascitic or hydrocele fluid or blood-serum, or a mixture of human blood-serum and bouillon. The addition of human proteids improves the media enormously, but it can be got to grow upon ordinary serum-agar. The addition of human urine also seems advantageous. The cultures usually die quickly, and in the case of the conjunctiva they are rapidly overwhelmed by other organisms, so that there is extreme difficulty in obtaining a pure culture.

Wilbrand, Saenger and Stachlin first drew attention to the importance of details in the diagnosis of the gonococcus in the conjunctiva, and their results were confirmed by Neisser. One cover-glass should first be stained by a simple aniline dye, *e.g.* Löffler's methylene blue, and then another by Gram's method, if diplococci are found. A convenient method of staining is Unna's, with a mixture of methyl green and pyronin;[1] the gonococci are stained red. It was

[1] Methyl green 0·15 gm., pyronin 0·25 gm., alcohol 2·5 c.c., glycerin 20 c.c., 2 per cent. carbolic acid to 100 c.c.

formerly considered final if decolorisation occurred with Gram, but Krukenberg found a diplococcus giving the same reactions in a case of slight catarrhal conjunctivitis. It was probably a meningococcus. It was distinguished from the gonococcus by the ease of cultivation on ordinary ox-serum, and its greater resistance to variations of temperature. The rarity of this organism scarcely vitiates the ordinary rules of procedure, but in cases of doubt cultivation experiments must be resorted to. Fränkel also found the *Meningococcus intracellularis* in three children. It did not decolourise so readily or so completely by Gram.

Pure cultures of the gonococcus or of blennorrhœal pus produce a purulent discharge when inserted in the rabbit's conjunctival sac (Groenouw).

There is evidence to show that the toxins of the gonococcus produce purulent conjunctivitis both in men and rabbits (Morax and Elmassian).

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THE KOCH-WEEKS BACILLUS

The commonest cause of acute contagious conjunctivitis seems to be the Koch-Weeks bacillus. It was discovered by Koch in Egypt in 1884, and was wrongly regarded by him as a concomitant of Egyptian ophthalmia. It was rediscovered by Weeks in New York in 1885, and proved by him to be the cause of an acute contagious conjunctivitis, which had no relationship with trachoma. Kartulis found it again in Egypt in 1887, and Wilbrand, Saenger and Staehlin in Hamburg in 1891. Since then it has been discovered almost everywhere—Morax (1894) in Paris, Juler (1894) in England, Gasparrini (1896) in Italy, etc.,—so that failure to find it in certain places by Gifford, Axenfeld, Fuchs, etc., is probably due to chance. It has been most thoroughly and most successfully investigated by Morax.

The bacillus mostly attacks young people—up to twenty years old,—but it occurs at all ages. It causes an acute muco-purulent conjunctivitis; no follicles are formed, but it frequently attacks the sufferers from phlyctenular conjunctivitis. The cornea is rarely affected, and then only by small grey superficial infiltrates; central

perforation has been described once (Morax and Petit). The pre-auricular glands are sometimes enlarged. It has been found in the new-born (Panas, Coppez); Coppez' case was pseudo-membranous.

The bacilli are best stained by fixing the film with sublimate, and subsequently washing out (less well by heat), and then treating with a carbolised solution of methylene blue or methyl violet. They are found lying between the leucocytes, and also within the protoplasm. They very nearly resemble the bacilli of mouse-septicæmia, but are thinner. They appear as very short fine rods (0·8—2 μ), staining less deeply than the nuclei of the cells (Fig. 20). They are often found lying end to end, so as to form chains of two or three links, or side by side. The ends are rounded, and often show a deeper polar staining. The number varies greatly according to the period and intensity of the

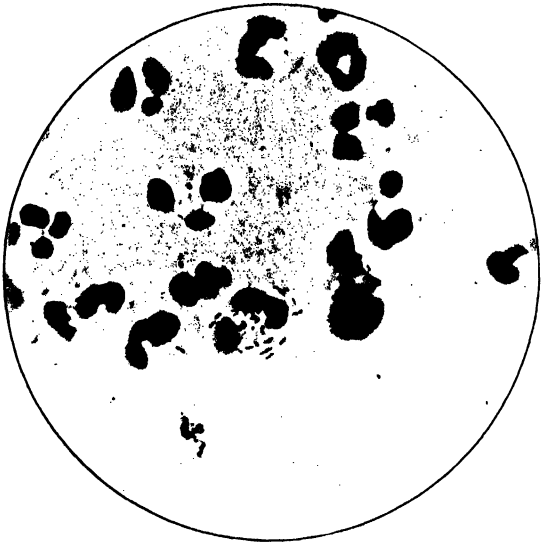


FIG. 20.—KOCH-WEEKS BACILLI. × 1000.
Photograph by Henderson. Film from conjunctival sac.

infection. They are often found in almost pure culture, but not infrequently diplococci are also present. In these cases it is not uncommon to find follicles in the conjunctiva (Wilbrand, Saenger, and Staehlin). They are decolourised by Gram's method. These characteristics render diagnosis by films easy.

Cultures are difficult, but a nearly allied form grows more easily (*v. infra*, Weichselbaum and Müller). The bacillus rarely grows on gelatine or serum, occasionally on agar (after two days), best on 0·5 per cent. agar, or the culture media most suitable for gonococci. It is essential that the agar should be very moist. The more virulent the conjunctivitis, the better are the cultures. Owing to the consistency of 0·5 per cent. agar, cultivation is best carried out in Petri dishes. After keeping at 35° Celsius, very fine, scarcely perceptible granulations appear on the surface after twenty-four to thirty-six hours. These

transparent colonies very much resemble those of the influenza bacillus. Besides these there are larger, greyish, more opaque colonies. These contain bacilli which stain with Gram, and generally show club-shaped involution forms. The club-shaped bacilli occur in other forms of conjunctivitis (ophthalmia neonatorum, etc.). They are easily isolated from the pure Koch-Weeks bacilli, but it is difficult to obtain the latter without the former (Greeff). It is best effected by inoculating the condensed water in a tube, and then making a second and third similar inoculation, finally spreading the water on the surface of the medium. Morax has succeeded in obtaining cultures on the ordinary media, but this usually fails. Subcultures always fail after the fifth day, and often before; Morax only obtained two or three generations on 0·5 per cent. agar.

The bacilli in cultures are non-motile, stain faintly with aniline dyes, and are decolourised by Gram. They cease to stain after a few weeks. They occur in clumps, and are mostly short, like those in the conjunctiva; but others, two or three times as long, occur.

Weeks failed to obtain positive results by inoculation in men and animals. Morax failed with animals, but succeeded with men. There is an incubation period of two to three days; the opposite eye usually becomes infected two or three days later. The inflammation reaches its height at about the sixth or seventh day. On the first day, only few bacilli can be found; after the third they are numerous; cauterisation with silver nitrate (0·5 per cent.) on the sixth day led to great diminution of the bacilli on the ninth day, and to total absence on the tenth day.

Microscopic sections of the conjunctiva, removed on the third day, showed ordinary lymphocytic infiltration, vascular congestion, and dilatation of lymphatics. The epithelium was intact. Sections stained by carbol-thionin and washed out with absolute alcohol (Nicholle's method) showed groups of bacilli in the superficial layers of the epithelium, and deeper amongst the leucocytes. There were none in the deeper tissues.

It is doubtful if the Koch-Weeks bacillus can give rise to a chronic conjunctivitis, but the investigations of Hoffmann, and of Weichselbaum and Müller tend to show that it can. The latter authors have obtained rather different results from Morax, chiefly with regard to details of cultivation. They compare the bacillus to that of influenza, and to Müller's trachoma bacillus (*v.* "Trachoma"). It is probable that the bacillus found by them is only a modified form of the Koch-Weeks bacillus.

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The Morax-Axenfeld Diplobacillus

The diplobacillus discovered independently in 1896 by Morax and Axenfeld is the cause of one of the commonest forms of catarrhal conjunctivitis. It occurs at all ages, but especially in adults. It is characterised by a chronic, not very severe blepharo-conjunctivitis, without follicles or membrane, but with a typical erythema of the edges of the lids, with slight maceration of the skin, most marked at the angles, especially the inner angle (*angular conjunctivitis*). The secretion is watery and not copious. Superficial infiltration of the cornea is not uncommon (Peters), and this also contains the organism (Morax and



Fig. 21.—Diplobacilli (Morax-Axenfeld). × 1000.
Photograph by Henderson. Film from conjunctival sac.

Petit, Petit [1]). The conjunctivitis is rapidly cured by zinc sulphate lotion, but shows no tendency to spontaneous cure.

The diplobacillus is apparently found in all countries, and is extremely contagious. Eyre found it in 2½ per cent. of all the patients in Guy's Hospital eye clinic, and it is equally prevalent elsewhere. Biard found it simultaneously in the nose. In 310 cases of catarrhal conjunctivitis Gonin found the diplobacilli 185 times, Koch-Weeks bacilli 10 times, pneumococci 10 times, streptococci 5 times, *Staph. aureus* 83 times.

Cover-glass preparations are quite characteristic (Fig. 21). The bacilli are generally very numerous; they are large (2 μ by 1 μ, but this varies considerably), generally occur in pairs, and often in chains. They are decolourised by Gram's method. They do not possess a well-defined capsule, but this is sometimes present (Gifford, Hoffman, zur

Nedden). A fine capsule can be demonstrated ordinarily by special capsule staining (Bietti).

Cultures are obtained with some difficulty, and only on blood-serum, serum-agar, or the usual media for gonococci. Blood-serum is liquefied. Cultures on serum-agar form minute transparent spots, not unlike pneumococcus cultures. The agar is not liquefied. The diplobacilli grow best on alkaline media, and are obligate aërobes; they are non-motile.

The diplobacillus of Morax is not pathogenic for animals, but is readily transferred from pure cultures to the human conjunctiva, the incubation period being about four days.

Allied to the Morax-Axenfeld bacillus is the *Bacillus liquefaciens* (Petit [2]). It is a diplobacillus, 1 μ—1·7 μ by 0·8 μ—1 μ, the diplo-form

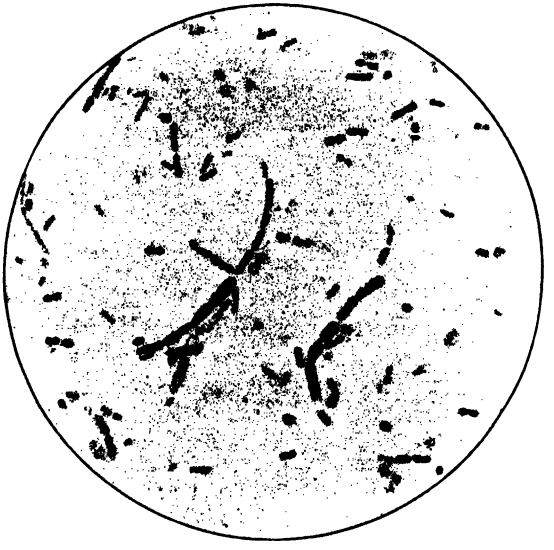


FIG. 22.—DIPLOBACILLI (Morax-Axenfeld). × 1000.

Photograph by Henderson. Culture, by Eyre, on serum-agar, eight days, showing involution forms.

being constant. It occurs in some superficial ulcers of the cornea, accompanied by slight iritis and hypopyon (McNab). McNab found capsules, which were not seen by Petit. It gives a negative reaction with Gram. It grows on all ordinary media, has a low power of resistance to heat, but considerable to dryness. It liquefies gelatin in stab cultures at 15°—20° C., but on cultivation this power appears to be lost (McNab). It rapidly liquefies blood-serum, in this respect differing from Friedländer's and zur Nedden's bacilli (q. v.). It differs from the Morax-Axenfeld bacillus in growing readily on pure agar.

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GIFFORD.—Annals of Ophth., vii, 1898. HOFFMANN.—A. f. O., xlviii, 3, 1899. LOBANOW.—A. f. O., li, 3, 1900. ZUR NEDDEN.—K. M. f. A., xxxix, 1901. PFLÜGER.—Korrespondenzbl. f. Schweizer Aerzte, 1902. BIETTI.—Ann. di Ott., xxviii, 2, 1899. PETIT (2).—Ann. d'Oc., cxxi, 1899; Recherches clin. et bactériol. sur les Infections aiguës de la Cornée, 1900. MCNAB (working under Axenfeld).—Personal communication; K. M. f. A., xlii, 1904.

THE DIPHTHERIA BACILLUS (KLEBS-LÖFFLER)

Membranous conjunctivitis was mentioned by Mackenzie in 1845, and possibly still earlier by Wharton Jones. It was not, however, until 1854 that von Graefe gave a satisfactory description of the severer type. It is a mistake to ascribe the account of the milder or croupous form to the earlier writers Bouisson and Chassaignac (1846) (Coppez [1]).



FIG. 23.—DIPHTHERIA BACILLI. × 1000.
Photograph by Henderson. Culture, by Eyre, on blood-serum, eighteen hours.

Babès, in 1886, first discovered the Klebs-Löffler bacillus in the conjunctiva.

The type of conjunctivitis caused by the diphtheria bacillus varies much; it is almost always membranous, but both its local severity and the severity of the general symptoms differ enormously. This is acknowledged by an overwhelming consensus of opinion. On the other hand, there is an equally wide agreement that membranous conjunctivitis (q. v.) is caused by many other agents, both chemical and bacteriological. In thirteen cases of membranous conjunctivitis Gonin found the Klebs-Löffler bacillus seven times, staphylococci four times, pneumococci once, and Koch-Weeks bacillus once. In most cases of true diphtheria, other organisms, especially staphylococci and streptococci, are found besides the Klebs-Löffler bacillus, and probably the nature of the mixed infection, combined with variability in the reaction

of the patient's tissues, determines whether the membrane will be merely superficial and benign, or deeply necrosing and malignant. It may even be absent; such cases are described in diphtheria epidemics, and in cases of membranous conjunctivitis in the other eye (Sourdille, Uhthoff, Aubineau, v. Hippel, Pichler, Coppez). The idea that the longer forms of the bacillus are most virulent (Martin) cannot be substantiated (Sourdille, Morax, etc.). There can be no doubt that the condition of the tissues is of great importance—that the diphtheria bacillus, in fact, is only conditionally contagious for the conjunctiva. This is seen clearly in rabbits, in which inoculation into the normal conjunctival sac fails if the epithelium is uninjured. Uhthoff, indeed, considers previous conjunctivitis essential in human beings, and eczema of the lids is common in the croupous form (Schmidt-Rimpler). The probability of Uhthoff's view is supported by Axenfeld, who points out that virulent diphtheria bacilli have been found on the normal mucous membrane of the throat. They have also been found in the conjunctiva (Coppez, Pichler). The bacilli persist for a long time during convalescence, and remain virulent (Sourdille, Uhthoff, Schirmer); repeated attacks may occur, probably owing to the passing off of a temporary immunity conferred by the previous attack. There is a rare chronic recurring form (Valude, Arlt, Coppez, Morton), which is only occasionally due to the Klebs-Löffler bacillus; staphylococci have been found, but the bacteriology has not been well worked out (*see* "Membranous Conjunctivitis").

Mixed infection, *e.g.* with streptococci, does not necessarily cause a severe type (Sourdille), but the majority of cases are worse than with pure diphtheria. Uhthoff almost invariably found staphylococci and streptococci, though the course of the disease was usually mild and uncomplicated.

There is now ample evidence to show that antitoxin treatment is very effectual in true diphtherial conjunctivitis (*e.g.* Jessop, Stephenson). Many, however, agree that it fails to produce amelioration of corneal inflammation, when that has supervened (Gonin, Uhthoff, Coppez [2], Wagner, Axenfeld). It has naturally been found to be less effectual in severe mixed infections (*e.g.* with gonococcus, Wagner). Morax and Elmassian have shown that membranous conjunctivitis can be produced in rabbits by dropping in diphtheria toxins, even without previous injury to the conjunctiva; the cornea is also affected (Coppez [3]). There is a definite latent period of twenty-four to twenty-eight hours. These results lend reason to the suggestion that the antitoxin serum should also be applied locally (Coppez [4], Mongour).

Randolph has found that continued instillations of the toxins of the *B. diphtheriæ* and of other organisms (gonococcus, streptococcus, *Staphylococcus aureus*, and *B. xerosis*), produced by filtration of sugar-free bouillon cultures of varying ages, produced no reaction on the normal conjunctivæ of rabbits. If, on the other hand, small amounts of the filtrates from even most recent cultures were injected into the tissue of the conjunctiva, marked inflammatory reaction followed. This tends to show that the bacteria are dependent in their action upon some lesion of the conjunctiva.

The subject is made more complex by the universal presence of the xerosis bacillus. The relationship of the two organisms will be discussed later.

The diphtheria bacillus was discovered by Klebs in 1875, but was only fully investigated, and proved to be pathogenic, by Löffler in 1884. It stains well with methylene blue, and is not decolourised by Gram's method. It is not quite so long as the tubercle bacillus, and rather thicker; but it occurs in very variable forms, straight or curved (Fig. 23). The extremities, which are more deeply stained, are often slightly enlarged; and this condition is often exaggerated by the formation of small, very deeply staining bodies at the poles, resembling spores. The bacillus, however, does not form spores.

It grows best upon Löffler's blood-serum,[1] but also well upon serum-agar, alkaline bouillon, etc. On solid media at temperatures from 20—42° C., it forms flat, greyish colonies in twenty-four hours. Involution forms are common in cultures, the bacilli appearing cut up into small rounded masses, some of which have a smaller diameter than the bacillus, others being larger and oval in shape. On glycerine agar the rods are shorter and thicker than usual. Both morphologically and physiologically—production of acid, indol formation, etc.—the bacilli vary greatly, and this fact probably accounts for many of the so-called pseudo-diphtheria bacilli. Special staining reactions, such as Roux' and Neisser's (*v. infra*), are by no means specific.

Subcutaneous inoculation of guinea-pigs with bouillon culture kills within thirty-six hours. A small patch of grey membrane is formed at the site of inoculation, with inflammatory œdema and hæmorrhages around.

COPPEZ (1).—Des Conjonctivites pseudomembraneuses, Bruxelles, 1897. BABÈS.—Prag. Med., 1886. GONIN.—Rev. méd. de la Suisse Romande, 1899. UHTHOFF.—Comptes rendus du XII Congrès internat. de Méd., Moskau, 1898; Vossius' Sammlung, ii, 5, 1898. SCHIRMER.—A. f. O., xl, 5, 1894. MORTON.—T. O. S., xiii, 1893. PICHLER.—B. z. A., xxiv, 1896. JESSOP.—T. O. S., xxii, 1902. STEPHENSON.—T. O. S., xxii, 1902. WAGNER.—Inaug. Diss., Giessen, 1898. AXENFELD.—Münch. klin. Woch., 1898. COPPEZ (2).—A. d'O., xix, 1899. MORAX AND ELMASSIAN.—Ann. d'Oc., cxxi, 1899; Verhandl. d. IX internat. Kongr., Utrecht, 1899. COPPEZ (3).—Verhandl. d. internat. Kongr., Utrecht, 1899; Z. f. A., ii, 1899, Beilageheft. COPPEZ (4).—Rev. gén. d'O., 1897. MONGOUR.—Ann. d'Oc., cxx, 1898. SOURDILLE.—Rev. mens. des Maladies de l'Enfance, 1895; A. d'O., xiv, 1894. RANDOLPH.—Bull. of the Johns Hopkins Hospital, xiv, 1903. BIETTI.—K. M. f. A., xli, 1903, Beilageheft.

THE XEROSIS BACILLUS (KUSCHBERT—NEISSER)

The so-called xerosis bacillus much resembles the diphtheria bacillus. It occurs extremely frequently in the normal conjunctiva, and in great numbers in xerosis; it is not, however, the cause of this complaint, but the conditions then present are very favourable for its development.

The bacillus was discovered by Kuschbert and Neisser in 1883 in twenty-five cases of xerosis in an orphanage at Breslau. It was discovered independently by Leber in the same year, and this discovery was confirmed by Schulz. Weeks, in 1887, failed to inoculate rabbits'

[1] Three parts calf's or lamb's blood-serum, with 1 part of peptone-bouillon made from veal and containing 1 per cent. grape sugar.

conjunctivæ from xerosis. Fränkel and Franke, in the same year, failed to transfer the disease from children to animals and children, but regarded the bacillus as the cause.

The xerosis bacillus is identical morphologically with the diphtheria and pseudo-diphtheria bacilli; it is stained by ordinary aniline dyes and grows on the same culture media, forming similar colonies. It differs from the diphtheria bacillus in not producing an acid reaction in neutral peptone-bouillon (Eyre), and, as we have seen, it is not pathogenic for men or animals. Fränkel regarded it as a non-virulent diphtheria bacillus, similar to those found in the throat by Roux and Yersin, which became virulent when mixed with streptococci; they failed to make this bacillus virulent by any method, but this result was also obtained in the case of very attenuated diphtheria bacilli. The failure to produce acid, described by Eyre, is only a question of degree, as the xerosis bacillus produces a small amount in time (Axenfeld). Like diphtheria, the bacillus varies in rapidity of growth and in form on various culture media; and, indeed, different forms occur in the conjunctiva. One of the most important of these, described by Gelpke as the cause of an epidemic acute catarrhal conjunctivitis and named the *Bacillus septatus*, has been the subject of much dispute (Heinersdorff [1], Axenfeld). Gelpke's results were founded upon 1559 patients; the catarrh showed typical swelling of the fornix as compared with relatively slight chemosis of the ocular conjunctiva ("Schwellungskatarrh"). A pseudo-membrane was rapidly formed, and corneal ulcers and iritis were common. The *Bacillus septatus* was found in all cases; morphologically and culturally the differences from the xerosis bacillus are minimal. Gelpke relies upon the fact that he has succeeded in transferring the infection to human conjunctivæ. He regards the catarrh as an attenuated diphtheria. Gelpke cannot be considered to have proved the identity of his organism.

Neisser, in 1897, described a method of staining which he thought definitely distinguished the xerosis from the diphtheria bacillus. Cultures are made upon Löffler's blood-serum at 35°; cover-glass preparations are made after ten to twenty-two hours' incubation; these are stained for one to three seconds with acetic acid methylene blue, and then for three to five seconds with Bismarck brown. True diphtheria bacilli are stained brown, and the polar globules described by Ernst are stained blue. The latter are not stained in xerosis bacilli. The difference is only one of time (Schanz), for xerosis bacilli react in the same manner after forty-six to forty-eight hours (Dötsch). Heinersdorff (2) investigated xerosis bacilli from sixty normal conjunctivæ, and never obtained the polar stain within twenty to twenty-four hours' cultivation. Fränkel considered that a negative result eliminated true diphtheria, though the converse did not hold good; he obtained a positive result once with a pseudo-diphtheria culture, and three times with a positive result the organism was not pathogenic for guinea-pigs. Löffler, however, at the International Congress for Hygiene in Madrid stated that the reaction sometimes failed with true diphtheria bacilli, and this has been confirmed. Staining of a few globules may be neglected; the characteristic polar staining must

be general. The positive reaction certainly seems to be very rare with xerosis bacilli, and it is so far useful as indicating treatment by antitoxin whenever it is found.

The resemblance between the xerosis and the diphtheria bacillus has led some to regard the former as merely a non-virulent type or stage of the latter, whilst others—and those the majority—affirm their independence. Schanz, who has paid much attention to the subject, objects to the term "pseudo-diphtheria" bacillus, and prefers to call it the non-virulent (*ungiftig*) Löffler bacillus. Practically all authors agree that the two cannot always be distinguished morphologically (Schanz, Heinersdorff, Axenfeld, Uhthoff, Pes, etc.). Similarly they are indistinguishable by culture, though the question of acid formation before referred to must be remembered, and the fact that the true diphtheria bacillus usually grows better on blood-serum, and more diffusely in bouillon. The universality of various pseudo-diphtheria bacilli must also be borne in mind. Hála has recently re-investigated the subject, and sums up in favour of the fundamental identity of diphtheria, pseudo-diphtheria, and xerosis bacilli ("coryna" or club-shaped bacilli).

The essential point is undoubtedly the question of virulence, and almost all authors agree with Schanz that virulent diphtheria bacilli are not infrequently found in slight cases of membranous conjunctivitis, whilst often only the non-virulent forms are found in severe cases. Any list of carefully investigated consecutive cases of membranous conjunctivitis will show this (*e. g.* Jessop, Stephenson, Pichler); few, however, will have the temerity to think that the Klebs-Löffler bacillus was present in all the cases, but overlooked in some (Stephenson).

Organisms belonging to the group of pseudo-diphtheria bacilli have been found by Leber and Addario in a case of congenital panophthalmitis in a goat.

Kuschbert and Neisser.—Bresl. ärztl. Z., 1883. Leber.—A. f. O., xxix, 1, 1883. Schulz.—A. f. O., xxx, 4, 1884. Weeks.—A. f. A., xvii, 1887. Fränkel and Franke.—A. f. A., xvii, 1887. Eyre.—Lancet, Dec., 1895; Jl. of Path. and Bac., 1896. Gelpke.—*Bacillus septatus*, Karlsruhe, 1898. Axenfeld.—In Lubarsch and Ostertag, 1901. Neisser.—Z. f. Hygiene, xxiv, 1897. Dötsch.—A. f. O., xlix, 2, 1900. Heinersdorff.—Centralbl. f. Bakt, xxiii, 1898; A. f. O., xlvi, 1, 1898. Fränkel.—Münch. med. Woch., 1898. Schanz.—Berl. klin. Woch., 1896, 1897, 1898; B. d. o. G., 1898; Deutsch. med. Woch., 1899; Z. f. Hygiene, xxxii, 1899. Bietti.—Ann. di Ott., xxvii, 1898; K. M. f. A., xli, Beilageheft, 1903. Pes.—Ann. di Ott., xxviii, 1898. Hála.—Z. f. A., ix, 1903. Jessop.—T. O. S., xxii, 1902. Stephenson.—T. O. S., xxii, 1902. Pichler.—B. z. A., xxiv, 1898. Leber and Addario.—A. f. O., xlviii, 1, 1899.

Other Micro-organisms

Other micro-organisms which have from time to time been found in the normal or diseased conjunctival sac are almost innumerable (*see* McFarland and Kneass). In many cases they are ordinary saprophytes, in others the results have never been confirmed. A few require passing mention.

McFarland and Kneass.—In Norris and Oliver, System, ii, 1897.

Bacillus coli communis.—It was only to be expected that this organism would be found in the conjunctiva. The credit of discovering

it there rests with Randolph, who found it in the pus from a case of traumatic panophthalmitis. It has been found since in ophthalmia neonatorum by Axenfeld, Cramer, Bietti, Groenouw, in pseudo-membranous conjunctivitis by Tailor, etc. zur Nedden proved it to be the cause of a case of hypopyon keratitis.

RANDOLPH.—Am. Jl. of Med. Sc., 1893. AXENFELD.—Korrespondenzbl. der Mecklenb. Aerztevereins, 1898. CRAMER.—Arch. f. Gynäkol., lix. BIETTI.—K. M. f. A., xxxvii, 1899. GROENOUW.—A. f. O., lii, 1, 1901. TAILOR.—Lav. d. clin. oc. di Napoli, iv, 1896. ZUR NEDDEN.—K. M. f. A., xl, 1902.

Bacillus influenzæ (Pfeiffer).—Cases of conjunctivitis due to the pseudo-influenza bacillus have been recorded by zur Nedden. It cannot be distinguished morphologically in smears from the Koch-Weeks bacillus (q. v.).

ZUR NEDDEN.—K. M. f. A., xxxviii, 1900; xli, 1903. JUNDELL.—Mittheil. aus d. Augenklinik, iii, Stockholm, 1902.

Bacillus pneumoniæ (Friedländer) was found in a case of pseudo-membranous conjunctivitis by Eyre, and has since been found rarely by Groenouw. v. Ammon obtained it occasionally in the conjunctival sac of new-born infants. It is probably identical with the ozæna bacillus (Löwenberg) (*see* " Dacryocystitis ").

BRAILEY AND EYRE.—Lancet, 1897. GROENOUW.—B. d. o. G., 1898; A. f. O., lii, 1, 1901. V. AMMON.—Münch. med. Woch., 1900. HIROTA.—*B. mucosus capsulatus*, Dissert. Halle, 1901. GOURFEIN.—Rev. méd. de la Suisse Romande, 1902.

Bacillus pyocyaneus has been found in several cases of purulent keratitis. Rapid sloughing of the cornea usually occurs, followed by panophthalmitis. In Sattler's two cases pure cultures of the *B. pyocyaneus* **a** were obtained; in two cases by Bietti and McNab the organism was the *B. pyocyaneus* β (Ernst). In all of these tests of virulence were carried out, and in all the organisms were extremely virulent. In McNab's case panophthalmitis and rupture of the globe followed inoculation of the rabbit's anterior chamber in forty-eight hours. Herbert has found the organism in cases of superficial keratitis (q. v.), but the variety was apparently relatively innocuous.

SATTLER.—B. d. o. G., 1891 and 1892. ERNST.—Z. für Hygiene, 1887. BIETTI.—Ann. di Ott., xxviii, 1899. MCNAB.—Ophth. Rev., xxiii, 1904; K. M. f. A., xlii, 1904.

INFLAMMATION

CONJUNCTIVITIS IN GENERAL

Conjunctivitis varies greatly in degree—from a slight hyperæmia with watery secretion, due chiefly to reflex secretion of tears, to an intense inflammation, with much swelling and a purulent discharge. It also varies greatly in duration, being transient or prolonged, according to the nature of the exciting agent. Anatomically, however, there are

certain features which are common to all forms, but which vary in detail according to the acuteness or chronicity of the process; whilst, superposed upon these features are others which are specific for certain types of conjunctivitis, and which often lie at the basis of clinical classification, *e.g.* follicular, membranous, etc.

The fundamental characteristics are for the most part those of inflammation in general. There is the same dilatation of blood-vessels and lymphatics, the same exudation of plasma, lymphocytes and leucocytes; the variations in detail depend solely upon the nature of the tissue. The substantia propria, consisting as it does of very loose tissue, affords little resistance to the outflow of fluid from the engorged vessels. Hence swelling (chemosis) occurs readily, though much of the



FIG. 24.—CONJUNCTIVITIS. × 10.

From a specimen by Stock (Freiburg i. B.). The eyeball and lids were removed post mortem from a case of pure diplobacillary conjunctivitis. Note the ectropion of the lid, and intense infiltration of the adenoid layer of the conjunctiva; the latter ceases on reaching the bulbar conjunctiva. (*See* K. M. f. A., xli, Beilageheft.)

fluid filters through into the conjunctival sac, mingles with the tears and secretions of the various glands, and forms the "discharge."

The adenoid layer already contains many lymphocytes, but these are enormously increased after a few hours' irritation, and further reinforced by polymorphonuclear leucocytes from the blood-vessels. This leads to great thickening of this layer, which becomes so packed with inflammatory cells that the supporting tissues are only seen with difficulty. The limits of the adenoid layer in the palpebral conjunctiva are well shown, the swelling ceasing at the sulcus subtarsalis. The fibrous layer is also infiltrated, but its denser framework prevents the same overcrowding of cells. The leucocytes wander still farther afield

and invade the epithelium, pushing their way between the cells; many succeed in reaching the free surface, and add their quotient to the conjunctival secretion.

The inflammatory cells consist of many different sorts. The small round-cells, or lymphocytes, are increased in numbers, probably partly by cell-division. They fill the perivascular and perineural lymph sheaths, and in these situations they often persist long after the original inflammation has subsided.

The polymorphonuclear leucocytes are wanderers from the blood-vessels, within which, also, they are present in abnormally large numbers. Free in the tissues, they adapt themselves to their surroundings, the nuclei apparently spreading out into filaments or networks, which have been regarded by Peters as coagulation products, though they stain deeply with nuclear stains.

Mast-cells (Ehrlich) also are increased in numbers. These are variously looked upon as leucocytes or as of connective-tissue origin. Since they occur in the blood (0·5 per cent. of the leucocytes), and are increased in myelogenous leukæmia, it seems probable that they are leucocytes. They are characterised by the presence in their cytoplasm of numerous small basophile granules. The nucleus is relatively small and irregularly trilobed. The cytoplasm is of irregular shape, with short thick processes; it is unstained by Ehrlich's triacid stain, but with basic dyes irregular dark blue clumps are seen. The granules are metachromatic, staining red with polychrome methylene blue, orange with Pappenheim's stain;[1] with Weigert's elastic-tissue stain they are bright red, with Weigert's fibrin stain blue.

Plasma-cells (Unna) are also found, and are greatly increased in all chronic inflammatory conditions. They resemble leucocytes, but are probably of connective-tissue origin (Unna), and indeed, play an extremely important *rôle* in the formation of scar tissue. Other authors regard them as derived from mononuclear lymphocytes. Their cytoplasm stains blue with methylene blue, whilst the nucleus, which is eccentrically placed, stains faintly, appearing as a clear spot with small irregular masses of chromatin situated chiefly on the nuclear membrane. The cytoplasm stains dark red with Pappenheim's stain, the nucleus dark blue, and the nucleolus red. Plasma-cells are found chiefly near the vessels, and especially in the adenoid layer.

The fixed connective-tissue cells are swollen. The interstitial connective tissue of the glands is infiltrated with round-cells if the inflammation is severe (Wolfring).

The epithelium shows an increase in goblet-cells, though this is not so marked as in chronic inflammations. The stasis in the blood- and lymph-flow leads to malnutrition, the epithelium suffering most. Many of the superficial cells are cast off, and the surface becomes irregular and loses its shiny appearance.

It also loses its transparency, so that the Meibomian glands can no longer be seen through it. This is due to the swelling, which also

[1] *Pappenheim's Stain.*—One part of methyl green—as much as will go on "the point of a knife"—to 2 parts of pyronin, in half a small test-tube of water. Stain five minutes, and then decolourise in 1 part of resorcin to half a test-tube of alcohol.

causes an increased roughness, the normal folds and furrows being exaggerated. The unevenness of the surface may cause only a velvety appearance, or may go on to papilliform projections. These are of colossal size in gonorrhœal conjunctivitis, in which the condition is most marked, and in which they are readily accounted for by the abnormal leucocytosis which takes place. In later stages true hypertrophy may occur, the fibrous tissue being increased and stretched, though the whole disappears eventually, and, in the absence of ulceration, there is no cicatrisation. This formation of false papillæ is quite different from that of true papillæ, as in spring catarrh (q. v.).

The secretion varies greatly in different types of conjunctivitis. At first it is watery and consists chiefly of tears, reflex secretion being increased. These are soon mixed with exuded plasma, which becomes mucoid by admixture with the secretions of an increased number of goblet-cells. Later, the addition of leucocytes makes the discharge muco-purulent or even purulent, according to the number of pus-cells. Hæmorrhages not infrequently occur, especially in pneumococcic conjunctivitis, and red corpuscles are then often found in the secretion. Epithelial and mucous cells are found, and many of the cells show fatty globules in their protoplasm. In the new-born, bile pigments may be present (icterus and ophthalmia neonatorum). In all cases many organisms are found, some of which may be specific.

Besides the papillary elevations in acute conjunctivitis, true follicles may be formed. When very small they give rise to the *vesicular catarrh* described by Arlt (Mayweg). They are confined to the tarsus. In the more pronounced form they cause *follicular conjunctivitis* (q. v.). In each case they are due to aggregations of round-cells.

Pustules may also arise around the cornea, but whether independently of phlyctenular conjunctivitis is uncertain.

In the later stages of subacute, and in chronic conjunctivitis, further changes occur in the epithelium. The number of goblet-cells is enormously increased, especially in the C. bulbi. They may be packed close together and form nests. The normal furrows are emphasised by the papillary formations, and are actually increased by active proliferation of the epithelium. In this manner gland-like tubular depressions are formed, often appearing to branch in all directions. They are probably formed by the canalisation of solid downgrowths, the central cells degenerating and disappearing. Their epithelium, being partially relieved from pressure, becomes glandular in type, and contains many mucous cells. The tubules never transgress the adenoid layer, and always have a definite basement membrane. A double layer of epithelium can usually be made out, so that they are not, at any rate for the most part, true glands. The mouths often become stopped up by agglutination, or by inspissated secretion and *débris*. In this manner a pseudo-retention cyst (q. v.) is developed later. It becomes filled with mucus, exudate, epithelial and leucocytic *débris*, in which calcareous deposits occur, with the formation of concretions (Fuchs, Wintersteiner) (*v. infra*).

In still more chronic conditions, especially when the conjunctiva is exposed to air and dust, as in ectropion, the epithelium changes its

character entirely, and becomes exactly like that of skin. Stratified epithelium replaces the normal kind; the middle layers form true prickle-cells, whilst the superficial ones are flattened, those actually on the surface losing their nuclei. Cornification of the cells, however, never seems to occur in the conjunctiva palpebrarum.

WOLFRING.—A. f. A., xxxi, 1895. PETERS.—C. f. A., xxi, 1897; K. M. f. A., xl, 1902. STOCK.—K. M. f. A., xli, 1903, Beilageheft.

Œdema of the conjunctiva occurs to a less or greater extent in all cases of conjunctivitis, leading to chemosis when it is extreme. Cases of angioneurotic œdema have been described (Black), as well as other aberrant forms (Holmes Spicer). These have not been submitted to microscopical examination. In many the ordinary inflammatory signs would doubtless be present, whilst the more chronic ones may be allied to cases of lymphoma (Guaita).

BURNETT.—A. of O., xxi, 1892. GUAITA.—Ann. di Ott., xix, 1890. BLACK.—Ophth. Rev., xiv, 1895. TERSON.—Recueil d'Opht., 1899. HOLMES SPICER.—T. O. S., xviii, 1898.

MEMBRANOUS CONJUNCTIVITIS.

We have already had occasion to refer frequently to membranous conjunctivitis. Like membranous inflammations of other mucous membranes, it is especially associated with the Klebs-Löffler bacillus, but it often results from the activity of other organisms, amongst which streptococci, gonococci, and pneumococci demand special mention. It is also found after burns, the application of strong caustics, *e. g.* lime, jequirity, etc.

A rare form of great interest is associated with herpes iris of the skin, though the skin eruption may be absent. This form is chronic, and in some cases recurs frequently; it has been recently investigated by Hanke. In one case Gehrke and Kain isolated a coccus which, inoculated upon a rabbit's conjunctiva, produced membranes there.

The membrane consists chiefly of a fibrinous network with leucocytes in the meshes. The epithelium is necrotic and separated, remnants of the cells being found in the membrane (Fig. 25). The raw surface bleeds when the membrane is removed, as in the true diphtheritic cases. If the membrane is not removed artificially it is raised by the development of granulation tissue, and undergoes hyaline degeneration, being finally cast off. It often develops again quickly, but when healing takes place the granulation tissue is covered with epithelium from the sides in the ordinary manner.

In the severer cases the subepithelial tissue also contains fibrinous networks, and the peripheral vessels, as well as being dilated, are often blocked with hyaline thrombi. Extensive necrosis may then occur: the fibrin undergoes hyaline degeneration, no longer staining with fibrin stains, and the same takes place in the connective tissue. Cicatrisation results in these cases in permanent scarring.

Cases of atypical, chronic membranous conjunctivitis previously

reported by Morton, Howe, Silcock and Maynard, Batten, etc., possibly belong to this category (*v.* p. 50).

MASON.—R. L. O. H. Rep., vii, 1873. FUCHS.—K. M. f. A., xiv, 1876. NETTLESHIP.—St. Thomas's Hosp. Rep., 1880. GUIBERT.—Soc. franç. d'O., 1893. BRONNER, MORTON.—T. O. S., xiii, 1893. *HOWE.—T. Am. O. S., 1897. BATTEN.—T. O. S., xviii, 1898. SILCOCK AND MAYNARD.—T. O. S., xx, 1900. GEHRKE AND KAIN.—A. f. A., xxiv, 1892. *HANKE.—A. f. O., lii, 2, 1901. ROSCHER.—K. M. f. A., xl, 1902.

TRACHOMA

Attention was first seriously directed to trachoma in Europe by the spread of the disease amongst the soldiers engaged in the Napoleonic wars. Vetsch (1807) first referred to the "*granulations*," which struck



FIG. 25.—MEMBRANOUS CONJUNCTIVITIS. × 130.

From a specimen sent by Prof. Fuchs. It is a case of herpes iris, and is probably from the case described by Hanke, and figured in A. f. O., lii, 2, 1901. The surface is formed by a layer of hyaline material derived from granulation tissue; the epithelium has been cast off. The tissue below this contains numerous very fine vessels, and is densely infiltrated with leucocytes; it is made up of young connective tissue with spindle-cells, and large oval cells with pale nuclei.

him as characteristic. Mackenzie described the epidemic upon the French slave-ship "Rodeur" in 1819. Memoirs relating to the epidemic followed from Larrey (1812), Rust (1820), v. Walther (1821), and Carl Ferdinand v. Graefe (1823). Among the various opinions held upon the subject in the early part of the century, the following may be mentioned:—J. Müller (1821), an affection of the mucous glandular tissue of the conjunctiva; Eble (1828), proliferation of the "papillary bodies," described first by him; Duvillards (1841) compared it with chilblains; Himly (1843), groups of small sarcomata; Hasner (1847), an herpetic eruption; Ruete (1854), a plastic exudation of the

submucous tissue; Lawrence (1850), actual warts; Pilz (1856), gelatinous exudates; Arlt (1856), "gelatinous exudates in the form of isolated granules."

Bendz, in 1858, first pointed out that the essential cause of the uneven surface of the conjunctiva was to be found in innumerable circumscribed aggregations of lymphoid cells. On account of their similarity to the solitary follicles of the intestines, he called them *lymph-follicles*. Two great discussions, which are not even yet settled, have arisen out of this discovery, viz. (1) whether lymph-follicles occur normally in the conjunctiva; and (2) whether follicular conjunctivitis and trachoma are one and the same disease or not.

From this time research was principally directed towards settling the exact nature of the trachoma follicle. In 1878 Berlin and Iwanoff published papers simultaneously, drawing attention to glands which they regarded as specific (trachoma glands). These were nothing more than the now familiar folds and furrows, Henle's glands, and new-formed inflammatory glands, which are met with under the most various circumstances. This was pointed out by Leber, and was clearly proved by a comparison with the normal conjunctiva by Jacobson.

In spite of many differences of opinion as to details in the structure of the trachoma follicle, nearly all observers agreed that it was impossible, on purely anatomical grounds, to diagnose between follicular conjunctivitis and trachoma. Saemisch (1876), however, drew a sharp distinction between them: "follicles" disappear, leaving no trace behind, "granulations" invariably leave scars; "follicles" are encapsuled, "granulations" have no capsule, and are genuine new formations. Raehlmann (1883, sqq.), at the opposite extreme, asseverates the identity of the two conditions. Sattler (1881) considers the trachoma follicle a thing *sui generis*, such as never occurs in the normal conjunctiva. Mandelstamm (1883) regards follicular conjunctivitis as the precursor of trachoma, the follicle being a mere filling of pre-existing lymph spaces under the stimulus of inflammation. Rhein (1888) supports Raehlmann on anatomical grounds, but these do not suffice to establish the identity of the conditions, as shown by Schmidt-Rimpler at the International Congress at Berlin (1890). It is perhaps easier for us in England to be convinced of the absolute duality of the two complaints, than for those, like Raehlmann, who work in dense trachomatous areas.

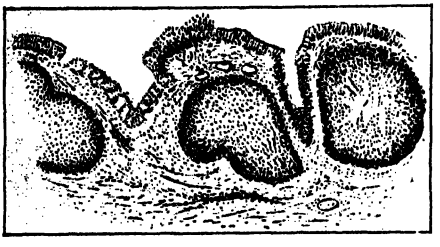


FIG. 26.—TRACHOMA, 1½ in. obj.
After Ridley (T. O. S., xiv, pl. i), showing the epithelium dipping down between the follicles.

Trachoma occurs in two forms: *papillary*, limited to the C. tarsi, in which the surface appears velvety from the formation and hypertrophy of pseudo-papillæ, which may form raspberry-like projections; and *granular*,

due to the formation of grey, translucent, hemispherical bodies, much resembling frog's spawn or grains of boiled sago. The latter are found chiefly in the folds of transition, arranged in rows like a string of pearls. In the C. tarsi the granules are also present, but owing to the adherence of the conjunctiva to the tarsus, they are smaller and bright yellow, or hidden by papillæ. These have been called "elementary or primary granulations" (v. Graefe, Jacobson), an unfortunate term, since they are not necessarily immature follicles, but are merely restricted in growth on account of their anatomical surroundings. Moreover they are especially characterised by a tendency to grow deeply and involve the tarsus, and are pathognomonic of trachoma, since follicles never occur here in follicular catarrh.

The granulations usually cease in a sharp horizontal line near the fornix, where the character of the epithelium changes, stratified epithelium being apparently unsuited to their development. They generally commence in the lower lid, either in the groove between the edge and the tarsus or near the fornix. They then spread to the angles, especially the inner, involving the caruncle and its neighbourhood. They grow similarly in the subtarsal groove below the upper tarsus, and reach their most profuse development above the upper tarsus, between it and the fornix. Growth upon the upper tarsus is latest, and, as mentioned, least striking.

Papillæ and granulations commonly occur together, the former most marked upon the tarsus, the latter in the fornices. Affection of the C. bulbi at the limbus follows, with the development of pannus trachomatosus (q. v.).

The papillæ and granulations ultimately retrogress, with the formation of fine cicatricial bands. These appear as narrow white striæ, forming a delicate network in the hyperæmic conjunctiva of the tarsus. They grow in number and breadth, invading the hyperæmic islands, until the whole becomes pale, thin, and smooth, the amount of cicatrisation corresponding with the amount of the hypertrophy. The white bands are less apparent in the fornices: here the conjunctiva becomes pale and flat, the normal folds being smoothed out and the conjunctiva seriously shortened. This shortening, combined with cicatricial changes in the tarsus, leads to entropion, whilst the earlier thickening and hypertrophy may cause ectropion, usually limited to the lower lid. The shortening may even obliterate the fornix and lead to symblepharon posterius; whilst the abolition of secretory functions may eventuate in xerosis or xerophthalmia.

The essential anatomical feature of all clinical types of trachoma, whether papillary, granular, mixed, gelatinous, etc., is the trachoma follicle, which is never absent, though it varies in detail.

The Trachoma Follicle (Fig. 26).—Arising from the discovery by Bendz in 1858 of the characteristic lymph-follicles is the question of their occurrence in the normal conjunctiva. As already stated (p. 34), they are normal in some animals, and poorly developed follicles are not uncommon in apparently normal human conjunctivæ. They are regarded as physiological by W. Krause, Baumgarten, Stöhr, etc.; and as invariably pathological by Waldeyer. In treating of so notoriously

unstable a tissue as lymphoid tissue, difficulty in arriving at a final decision is not surprising. Suffice it to say that trachoma is accompanied by an enormous and wide-spread development of such follicles. Here they form larger or smaller nodules, varying much in appearance according to age and size. They lie in the adenoid layer, and lift up the epithelium above them.

Wolfring (1868) came to the conclusion that follicles do not occur normally, but that they are the essential feature of trachoma. They occur in the pre-formed adenoid layer of the conjunctiva, and, like those of the intestine, consist of (1) a stroma, viz. the reticular tissue of the adenoid layer of the conjunctiva; (2) lymphoid elements in the meshes of the stroma; (3) vessels, which surround the follicle, and send sparse capillaries into it; and (4) an inconstant fibrous-tissue capsule. Thus early were the essential elements of the trachoma follicle described, but each of these constituents has been the field of heated controversy.

1. *The stroma.*—Whilst most authors agree as to the existence of a stroma, they differ as to its distribution and constitution.

Jacobson describes a fine network which pervades the inflamed area and extends to the tips of the papillæ, enclosing the infiltrating cells in its meshes. It is best seen by hardening in chromic acid, or in Müller's fluid and alcohol, or in alcohol alone; and parts can be seen well in teased preparations. By pencilling out the enmeshed cells in thin sections a fine reticulum is obtained, at the nodal points of which nuclei are often seen. The meshes are smaller and longer at the periphery of the follicle, and wider near the centre. Jacobson's description agrees with the earlier ones of Blumberg, Berlin, Iwanoff, and with the later ones of Sattler, Raehlmann, v. Michel, etc. Raehlmann describes a distinct network in young follicles, consisting of branching fibres with nodular or stellate swellings at the divisions, the latter often having pale oval nuclei.

Mandelstamm (1883) denied the presence of a stroma, and attributed the appearances to fine branching processes of the cells, which interlocked and simulated a reticulum.

Villard (1896) and Pick (1897) also deny that there is a stroma, the reticulum being an artefact, due to coagula. There can be no doubt that there is a stroma in the periphery of the follicles, and that this increases very markedly with age. The fibrous tissue here contains fixed connective-tissue cells, mostly spindle-shaped or stellate, with pale, round, oval, or long nuclei. Villard finds that few fibres pass inwards from this peripheral capsule, and that these belong chiefly to the vessels, adhere to them, and have only a few long nuclei. One often sees a very fine network with narrow meshes in the centre, especially in preparations fixed with Flemming's solution. This has no nuclei, and is due to coagulation. Pick agrees with these conclusions; he never found a reticulum in fresh follicles, even by pencilling out the cells. He compares the coagula with those found in other pathological processes, *e. g.* coagula of blood proteids in tubercle (Schmaus and Albrecht), but this does not seem a very fortunate analogy.

Addario (1900) cut serial sections of young nodules, and found that

the faintly stained centre contained many cellular elements, lying fairly far apart, so that an intercellular stroma could be clearly distinguished. This sprang from the peripheral strands, which continually divided as they passed inwards, until they finally enclosed only two or three cells, and even these were separated by fine protoplasmic processes of the connective-tissue cells. These results support those of Moauro (1891), and are opposed to those of Villard and Pick. Towards the periphery of the young nodule the fixed cells are small and spindle-shaped; where the fibres divide they are often triangular. Other large cells—the trachoma corpuscles—Addario considers to be fixed connective-tissue cells (*v. infra*).

The arrangement of the fibrous tissue is best seen in sections stained by van Gieson's method. The fuchsin-stained fibres are then seen to be almost limited to the peripheral parts.

2. *The cells.*—Jacobson and Sattler distinguished two types of cells: quite small lymphoid cells, with small, round, deeply stained nuclei; and much larger cells, with large, round, pale nuclei, which are distributed more or less regularly through the follicle. The smaller cells are closely packed at the periphery, so that a deeply stained peripheral zone is usually well marked off. The larger cells are scattered amongst the looser small cells in the interior, which therefore looks paler.

Villard further subdivided the cells thus:—(*a*) Lymphocytes, arranged in typical fashion, or forming small secondary nodules; (*b*) mononuclear leucocytes of varying size, and often epithelioid, forming the main mass of the follicle; (*c*) large cells of unknown origin, found sparsely in the middle of the granulation, with a voluminous nucleus and a large cell-body; they have protoplasmic processes which unite with those of other cells, and form a network within the reticulum; (*d*) phagocytes, voluminous cells of varying shape, with different cell-inclusions, doubtless products of metabolism; (*e*) accessory elements, multinuclear cells, eosinophile cells, polymorphonuclear leucocytes, etc. (*c*) and (*d*) are probably identical, and will be considered together.

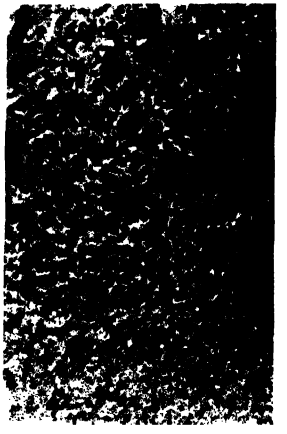


FIG. 27.—TRACHOMA.

Herbert, T. O. S., xix. Portion of a trachoma follicle, stained by Unna's protoplasm method. Lymphocytes are seen as rings amongst the *débris* of broken-down ...

(*a*) *Lymphocytes* (Fig. 27).—These are small mononuclear cells, with little cytoplasm. The nucleus measures 4—7 μ, and stains very deeply. They never show karyokinetic figures. The lymphocytes form the chief constituent of the peripheral zone, and are arranged here in rows between the connective-tissue fibres. They are few in the centre, but increase in numbers in cicatrising follicles (Pick). At the edge of the follicles the lymphocytes and their nuclei are sometimes seen much elongated, giving evidence of amœboid movements, the cells being

caught in the act of streaming out into the surrounding tissues (Herbert). It is questionable whether these are not polymorphonuclear leucocytes.

(*b*) *Mononuclear leucocytes* (Fig. 28).—These are the characteristic cells of the follicle. They have well-marked cell-bodies (16—18 μ), which are round, or polygonal by mutual pressure. They often appear epithelioid, especially in preparations hardened by Flemming's solution. Their nuclei measure 7—12 μ, stain faintly, and often show karyokinetic figures. The larger the nucleus the fainter it stains, and degeneration of the nucleus apparently occurs when a certain size is attained (Leber). The nucleus is always granular, and some cells have quite small nuclei, about one fifth the usual size. These cells may be regarded as different stages of the peripheral lymphoid cells (Addario) (lymphogonia, Benda). Herbert compares the epithelioid cells with plasma-cells, with which they have many points of resemblance. The cytoplasm is less, but stains darkly with basic dyes. The nuclei of the larger cells show several large nucleoli. When the protoplasm is stained with polychrome methylene blue two or more closely packed nuclei may be made out, probably due to amitotic division (Herbert). Whilst resembling plasma-cells, they are not identical; typical plasma-cells do not occur in the follicles, but are found in the diffuse infiltration. In places rows of plasma-cells are found close beneath the epithelium, separated by bundles of fibrous tissue (*cf.* Fig. 37). These are Leber's half-moon cells (*v. infra*).

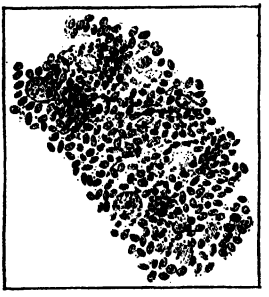


FIG. 28.—TRACHOMA. Zeiss D = ⅛ in. Obj.

After Ridley. Part of a trachoma follicle, showing epithelioid cells.

Division of the epithelioid cells gives rise to the lymphocytes, all transitions being seen in a follicle (Herbert). Even in the boundary zone, and in the accumulations in lymph vessels, where the smallest lymphocytes are found, there are always a few epithelioid cells.

(*c*) *Large cells* (*phagocytes* [Villard, Pick], *large connective-tissue cells* [Addario], *Körperchenzellen* [Leber], *trachoma corpuscles*) (Fig. 29).—These are much larger cells, often very numerous, scattered about the interior of the follicle. They have a large irregular cell-body, with long protoplasmic processes. The round or oval nucleus is very large, pale, and homogeneous, with one or two nucleoli. The cytoplasm contains vacuoles and very various cell inclusions, *e. g.* fragmentary nuclei, red corpuscles, pigment, etc., often in grotesque shapes.

Omeltschenko considered that they must be derived from epithelial cells. Pick, on the grounds of general pathology and the differences exhibited by granulation-tissue cells, regarded them as derived from cells of the conjunctival stroma or from endothelial cells of the vessels.

Addario considered them fixed connective-tissue cells. Some adhere to the fibres of the stroma; others are irregularly star-shaped, and only touch the fibrous tissue by their processes; in others the long

thin processes extend far from the cell-body. The cell-inclusions are always surrounded by a small clear zone. These cells are always found in the first stage of development of the follicle, and become fewer later. Their relationship to the reticulum points to their connective-tissue origin, and intermediate forms between them and the fixed cells are common. These are long oval cells, with pale oval homogeneous nuclei, with a nucleolus. Where the fibres divide, the large cells are often triangular, and their processes cling to the fibres. Similar cells were found by Flemming (1885) in normal lymphatic nodules, and by Moauro in trachoma in 1890.

Leber very wisely called these cells "Körperchenzellen," on account of their cell-inclusions, a name which did not prejudice any theory. He remarks that Pfeiffer (1894) probably referred to these when describing

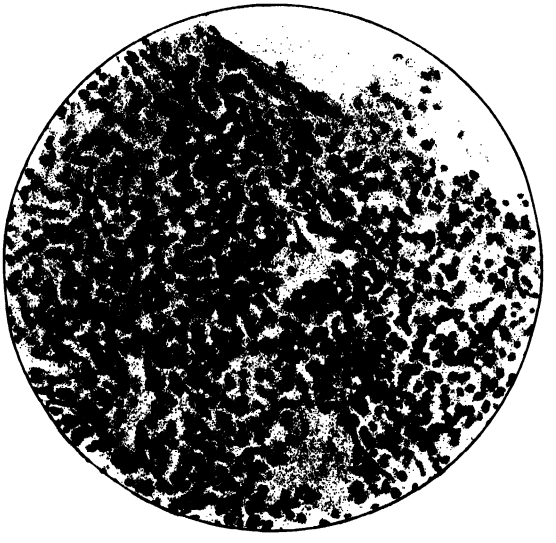


FIG. 29.—TRACHOMA. × 260.

From a specimen by Herbert. The triangular cell in a large space near the centre contains amorphous hyaline granules; below this and a little to the right is a cell containing globules of hyaline material.

some parasitic appearances which he found both in vaccine-inoculation of the cornea and in trachoma. Leber found them in other lymph-follicles of the conjunctiva; and they were also found by Heidenhain in the mucous membrane of the intestine, and by Hoyer in lymphatic glands.

Greeff was struck by their resemblance to Protozoa, and showed them to specialists, who were surprised at the resemblance. Greeff says that they are not found outside the follicles. This, however, is not true. Herbert has found them in diffuse lymphoid infiltration, but here the cells are not so swollen, the cell-inclusions are not collected into groups, and without special staining are liable to be overlooked. The inclusions are hyaline bodies; some are perfectly spherical globules formed in swollen plasma-cells (Fig. 29); others are angular, formed in long

connective-tissue cells. In any case the "Körperchenzellen" are of connective-tissue origin (Herbert).

(*d*) *Accessory elements.*—These are inconstant constituents of trachoma follicles, and include the following:

(α) Polymorphonuclear leucocytes are found rarely; they are evidence of pyogenic infection.

(β) Mast-cells are found at the periphery, especially of large follicles. They are a normal constituent of the conjunctiva.

(γ) Villard found large cells with eosinophile granules in a single case.

(δ) Giant-cells have occasionally been found (Villard, Pick). They have from three to six large, deeply staining nuclei in a small mass of cytoplasm, and probably arise from the epithelioid cells by nuclear division without cell-division (Pick).

(ε) Irregular, deeply staining fragments of nuclei are often found scattered in the follicle.

It may be noted that all these cells are of mesoblastic origin, none being derived from epiblast (Villard).

The youngest or "*initial*" nodule consists of a minute round aggregation of cells, about 0·24 mm. (Addario) or 0·3 mm. (Villard) in diameter. The distinction between the darker peripheral zone (0·65 mm.) and the clearer centre (0·20 mm.) is very early apparent (Addario). The clear part (0·16 mm.) possesses all the characters of an ordinary lymphatic nodule, consisting of epithelioid cells with large nuclei, many of which are undergoing mitosis. Some of these contain cell-inclusions. Blood-vessels, which are absent in the youngest nodules, may be seen developing, but the stroma is seen with difficulty, owing to the crowding together of the cells. The periphery contains smaller cells than the centre, and these have granular, deeply stained nuclei. They are much more numerous than in the initial nodules, but the stroma can be made out continuous with the connective tissue of the surrounding conjunctiva.

As the nodule increases the central part grows much more rapidly than the periphery, having a diameter of 0·35 mm. in a nodule of 0·40 mm. Karyomitoses are numerous. The surrounding fibrous tissue, which is looser in the periphery of the smaller and closer in that of the larger nodules, forms no true capsule, but is in direct continuity with the submucosa.

In nodules of 0·96—1·28 mm. the trachoma corpuscles contain many more cell-inclusions than in the smaller nodules. These consist principally of degenerated nuclei (Addario), but this is denied by Flemming for lymphatic nodules and Peyer's patches, their true nature being as yet undetermined. Some contain two unequal nuclei, possibly due to fragmentation. Others contain pigment granules, as was also found in lymphatic nodules by Flemming. The pigment is probably the result of the intra-cellular destruction of red blood-corpuscles.

A small number of long, irregular, polynuclear cells with very little protoplasm may be seen; they consist of little more than groups of two, three, or more, pale homogeneous nuclei, each with a nucleolus. They are probably young connective-tissue cells, or precursors of the trachoma corpuscles (Addario).

3. *The vessels.*—Blood-vessels were described in the follicles by Wolfring, and this was confirmed by Blumberg, Jacobson, Sattler, Leber, etc. Iwanoff alone failed to find them. Raehlmann found the follicles poor in vessels, v. Michel only vascularised at the periphery, and Villard very richly supplied.

The fully developed follicles have a rich network of blood-vessels around them, from which numerous capillaries pass inwards, disappearing towards the centre. They are very thin-walled, with an endothelial lining, and rarely muscle-fibres (Pick). Probably they are early obliterated, thus aiding resolution (Greeff). Old soft follicles often have degenerated and obliterated vessels.

Authors differ as to the relative proportion of lymph-vessels. Villard's contention that the follicles lie in the course of lymph-vessels is of great importance as regards their true status as lymph-follicles.



FIG. 30.—TRACHOMA.

Herbert, T. O. S., xix. Origin of a trachoma follicle in a lymph-vessel. A. Collection of small lymphocytes in a lymph-vessel. B. A less defined group of lymphocytes. *a, a.* Larger cells undergoing mitosis. C. Thickly distributed large plasma-cells. D. Epithelium.

This theory is supported by Herbert (Fig. 30). Probably the smaller nodules are entirely nourished by lymph. It is certain that the lymphatics below and upon the surface are often widely dilated, and packed with leucocytes. The superficial ones explain the so-called "vesicular granulations" of the older authors (Raehlmann), and are rarer than the deep dilated ones. Lymphatic spaces with an endothelial lining cannot usually be made out within the follicle.

4. *The capsule.*—The existence of a definite capsule was affirmed by Wolfring, and confirmed by Blumberg, Berlin, and Iwanoff. Jacobson and Raehlmann found no true capsule, but special small peripheral cells, which, according to the latter author, became changed into spindle-shaped cells and fibres. Such a metamorphosis of lymphoid into connective-tissue cells is contrary to general pathological teaching.

Saemisch denied any capsule to his "granulations," whereas "follicles" have capsules.

The periphery of the nodules is distinctly marked off by the zone of lymphocytes, arranged in concentric rows. There is connective tissue between these cells, but it forms no true capsule. It surrounds only that part which impinges upon the submucosa, and sections may be seen which give the appearance of a complete sheath. Serial sections, however, show that this consists of submucous fibrous-tissue bundles, which are distorted and displaced. In fact, they run continuously over the nodules, and on the surface of the conjunctiva they run parallel to the adenoid layer (Addario). In these respects the granulations differ in no degree from lymphatic nodules. The bundles are separated from one another by the infiltrating cells rather than pressed together by them (Greeff).

As the nodules become older a true capsule is undoubtedly formed, which reaches its maximum in the regressive stages. This is the commencement of cicatrisation; it does not usually develop equally in the periphery, but begins on the deeper surface.

The epithelium.—The epithelium is usually thickened, both on the surface of the papillæ and granulations, and also in the depressions (Fig. 31). True papillæ are often superposed upon the pseudo-papillæ formed by the folding of the increased area of the conjunctiva. In the depressions the normal duplex layer of epithelium is maintained, but on the summits the cylindrical cells are lost early (Fig. 33). They are replaced by layers of rounded (deep) and flattened (superficial) cells derived from the basal cells, which assume a cubical or even cylindrical form, and show many karyomitoses. The overgrowth of epithelium in itself conduces to the formation of cockscomb-like sprouts. Rarely the epithelium becomes quite like that of the epidermis, with the development of a superficial corneous layer (Baumgarten). In such cases the cells of the middle layer are prickle-cells with intercellular lymph-channels in which leucocytes are often found (Villard). The goblet-cells are much increased (Fig. 32), especially in the depressions, and the whole epithelium is pervaded with leucocytes.

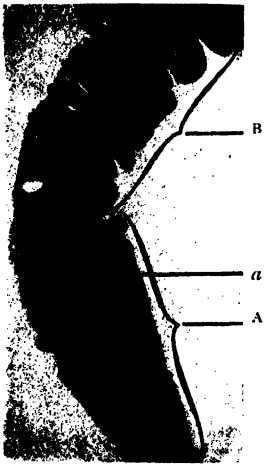


FIG. 31.—TRACHOMA.

Herbert, T. O. S., xi Upper palpebral conjunctiva in very chronic trachoma. A. Marginal strip, reaching up to the sulcus subtarsalis, with thick stratified epithelium resembling epidermis. *a*. Tarsus. B. Lymphoid portion, showing a tendency to papillary formation, numerous epithelial downgrowths, and small-celled infiltration.

Follicles do not occur where the epithelium is normally stratified. This is doubtless due to the fact, insisted upon by Mutermilch, that adenoid tissue is not found immediately beneath epidermoid epithelium anywhere in the body. Mucous epithelium is specially constituted for secretory purposes, and demands a rich vascular and lymphatic supply.

The active regeneration of this epithelium under the influence of irritation may become excessive, leading to a change in type. In this manner its powers of resistance are increased, and a new balance is set up between the epithelium and its substratum (Mutermilch), at the loss, however, of its proper secretory function, and the development of conditions allied to those of skin.

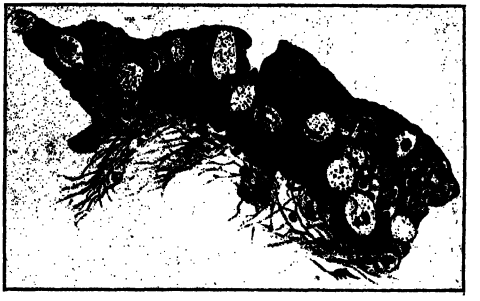


FIG. 32.—TRACHOMA. Zeiss E = ⅛-in. Obj. After Ridley. Epithelium from the fornix, showing goblet-cells. Prepared by Foa's method.

Necrosis of the epithelium was described by Remy over the follicles. This only occurs as a secondary phenomenon by the mechanical pressure of the growing follicle, whereby the basement membrane and epithelium are injured and caused to degenerate. Ulceration, described by Raehlmann as a frequent precursor to resolution, probably does not happen. The epithelium is often mechanically broken, but rapidly heals.

Solid epithelial downgrowths are either the result of healing of such excoriations (Raehlmann, Nuel), or more probably are due to inflammatory hyperplasia.

Gland-like depressions are enormously increased. These are mostly folds and furrows (Henle's glands), but true tubular glands are also formed, as in so many inflammatory conditions of the conjunctiva (Fig. 33). Attention was unduly directed to these structures in 1878 by Berlin and Iwanoff, who regarded them as the essential features of the disease (Berlin and Iwanoff's trachoma glands). Berlin thought that they were developed from pre-existing glands, whilst Iwanoff thought they were new formations. Their relation to trachoma is in no sense specific, but the actual increase of true tubular depressions in this and allied conditions must be admitted. The mouths of these depressions readily become blocked mechanically, and in this manner the mucus, leucocytes, shed epithelial cells, and other *débris* are retained within the lumen. This becomes dilated, and *cysts* are formed. These may also be due to the degeneration of the central cells of solid epithelial downgrowths (Fig. 34). The smaller ones are lined with a double layer

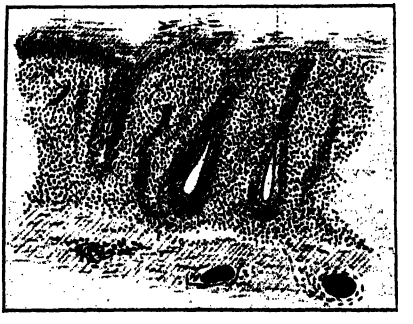


FIG. 33.—TRACHOMA. Zeiss AA = ⅔-in. Obj. After Ridley. Showing deepening of the crypts. Most of the epithelium has gone, except at the blind ends; what remains is infiltrated with leucocytes.

of epithelium, the inner being cylindrical, with many goblet-cells. These contain coagula, granular *débris*, and leucocytes with badly staining nuclei. The larger ones may be several millimetres in diameter, and are then lined with flattened epithelium, and are often empty or contain a clear fluid (Fig. 35). The cysts are usually surrounded by an inflammatory thickening of the fibrous tissue, which forms a capsule.

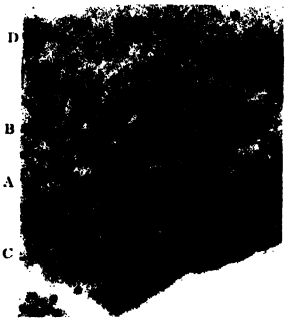


FIG. 34.—TRACHOMA.

Herbert, T. O. S., xix. Origin of a conjunctival cyst from an epithelial tubule. A. Epithelial lining. B. Collection of cells, mostly wandering cells, distending tubule. C. Epithelial lining of a large cyst. D. Surface epithelium (out of focus).

The crypts and crevices in the trachomatous conjunctiva must afford an excellent site for the materies morbi, and add greatly to the difficulty of eradicating the disease.

Changes in the surrounding conjunctiva.—These vary greatly in degree, but are always present, trachoma thus differing from follicular conjunctivitis. They consist chiefly in wide-spread infiltration with lymphocytes, especially of the adenoid layer, accompanied by œdema. Besides lymphocytes, plasma-cells, mast-cells, and "half-moon" cells (Leber) are found. Plasma-cells are found in enormous numbers beneath the epithelium, and even in the discharge (Mayou). Mast-cells were found particularly in trachoma by Fuchs, but are in no way specific (*v.* p. 56). "Half-moon" cells are mononuclear cells, the nucleus of which is pressed to one side of the cell and is half-moon or sickle-shaped. The neighbouring protoplasm is more deeply stained, the remainder very faintly stained. The concavity of the crescent is always directed towards the surface of the conjunctiva. Polymorphonuclear leucocytes are often present in numbers in the adenoid layer. They may lead to the formation of deeply-staining networks like those described by Peters (*v.* p. 56).

After the disappearance of the œdema new vessels appear in the papillæ, with numerous capillary loops. Fibrous tissue develops along the walls and contracts, the papillæ shrinking, whilst folds long remain to mark their position.

Cicatrisation.—Trachoma invariably ends in cicatrisation, but the method whereby this takes place is a matter of dispute, and probably varies. Most commonly it is by absorption of the contents of the follicle and proliferation of the connective tissue of the conjunctiva; there is little evidence that the elements of the follicle can themselves form fibrous tissue to any considerable extent. Less frequently the contents of the follicles are expelled into the conjunctival sac, and the resulting "ulcer" or wound is healed by cicatrisation. Raehlmann, Addario, and others attach an undue importance to this method.

Resorption can apparently occur at any stage, by mere retrogression, without softening. This must be regarded as exceptional. Usually degenerative changes occur in the cells. The large cells necrose, their nuclei no longer staining, the cytoplasm becoming granular. This

generally begins in the centre, but foci may be dotted about. The cells finally break down into a granular mass, and spaces are formed, separated from each other by the more resistent fibrous tissue. The blood-vessels at the periphery and in the neighbouring conjunctiva are often sclerosed, with thickened homogeneous walls, and finally obliterated lumina (Raehlmann). This process may be the cause of the necrosis.

Where the follicles are very thickly set softening may lead to fusion, and may extend to the adenoid layer and epithelium in the form of fatty or hyaline degeneration. The clinical picture is then characteristic, and has led to the term *gelatinous trachoma* (Stellwag). The epithelium then often gives a mahogany-brown coloration with iodine,

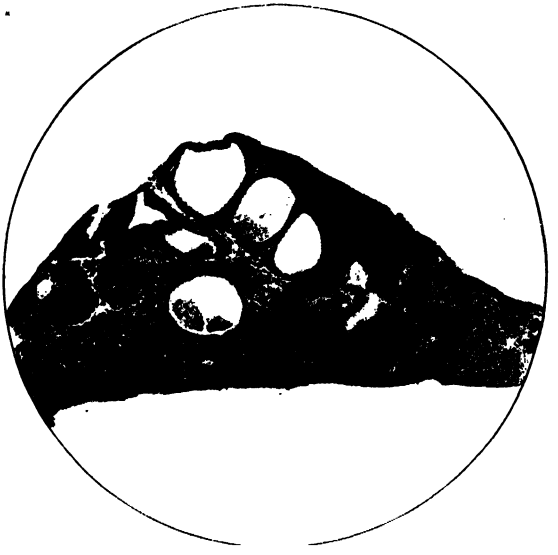


FIG. 35.—TRACHOMA. × 34.
From a specimen by Herbert. Cysts in upper palpebral conjunctiva.

but it is probable that the true amyloid degeneration of the conjunctiva is wholly independent of trachoma (Raehlmann, Reymond, Kubli, Vossius) (*v. infra*).

It is probable that in many cases the process of resorption is slower, and the degenerative changes are less marked. The new growth of fibrous tissue is then the more prominent feature, and the process is one of slow induration rather than softening. In rare cases, indeed, simple absorption with a minimum of scarring—though always some—may occur (Greeff).

According to Raehlmann, Addario, and others, the softening generally involves the adenoid layer, which shows fatty degeneration. The epithelium becomes thinned and finally broken through, and the follicle opens on to the surface. The contents are gradually extruded, the process being aided by movements of the lids, etc. The walls then fall together, the space being rapidly filled with granulation tissue,

which finally forms a compact scar. This method cannot occur in those cases in which a complete capsule of fibrous tissue is gradually built up, and is probably exceptional in all cases.

Addario is doubtless right in deriving the new fibrous tissue chiefly from the adventitia of the blood-vessels (*cf.* "Retina").[1] It accumulates at the periphery, first on the under surface, finally encapsuling the follicle. Gradually it encroaches more and more upon the centre, the specific cells disappearing before it. These are at last almost confined to the centre, and are even here pervaded by bold bands of fibrous tissue. As the fibrous tissue contracts, so the follicle shrinks. Most commonly the process is not confined to the follicles, but invades the whole neighbourhood of the conjunctiva, the connective tissue proliferating, contracting, strangling the vessels, and eventuating in compact scar tissue, no trace of follicles being finally left.

Changes in the tarsus, etc.—Histological changes in the tarsus were first described by Wolfring, viz. nests of lymphocytes amongst the fibres. Raehlmann considered that the distortion of the tarsus was mainly due to contraction of the conjunctival scar. Most authors, *e.g.* Saemisch, v. Michel, Fuchs, Greeff, etc., think that there is usually a primary affection of the tarsus, and Raehlmann now admits this in some cases. The tarsus is usually bent so that the convex surface looks forwards. This, according to Raehlmann and Pick, is due to the thickness and contraction of the conjunctival fibrous tissue on the inner surface, the union between the two being normally very firm. There is no necessity for the tarsus itself to be inflamed. Sometimes the fibrous tissue of the tarsus contracts *pari passu* with the scar tissue, and the tarsus then shrinks in size without becoming bent. This occurs particularly in the severer forms of trachoma, *e.g.* gelatinous trachoma, in spite of the extreme swelling of the lids which happens earlier in these cases (Raehlmann). The bending is most marked when the middle of the tarsus is softened by the follicular process, the edges remaining firm. Where the tarsus atrophies it may, like the scar itself, be replaced by a loose reticular tissue containing fat.

In the earlier stages it is the rule to find the tarsus invaded by round-cells, including mast-cells, which find their way along the blood-vessels and lymph spaces, especially in the neighbourhood of the upper and lower arterial arches.

All the tarsal glands are affected by the process, especially the Meibomian glands. As long as the follicles are limited to the fornices, the Meibomian secretion is not altered. When they invade the C. tarsi, the secretion becomes grumous and frothy. The bending of the lid leads to ectasia of the ducts, whilst the acini may still continue to be functional. Later the acini atrophy, first in the upper lid, being to a large extent strangled by the overgrowth of bands of fibrous tissue. Many of the acini degenerate into cystic spaces, lined with irregular cubical epithelium. The irritation sometimes leads to the formation of groups of giant-cells in the vicinity. Other acini become filled with cells, whilst many disappear entirely and are replaced by fatty

[1] Parsons, R. L. O. H. Rep., xv, 3, 1903.

connective tissue. The follicles in rare cases invade the edge of the lid, and thus lead to implication of Moll's glands; the cysts are then more frequently quite denuded of epithelium.

Pick showed that the infiltration of the conjunctiva extends deeply in the fornix, where the submucous tissue is loose; it may extend as far as between the muscle bundles. Raehlmann says that Krause's glands are often colossally hypertrophied, the hypertrophy corresponding in degree with the atrophy or loss of function of the Meibomian glands. They seem, therefore, to act in some degree vicariously.

Cicatrisation leads to displacement of Krause's glands, so that they usually come to lie behind the middle of the lid. Infiltration of Krause's glands may also occur, probably more commonly, followed by partial or complete atrophy and the formation of cysts.

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The Bacteriology of Trachoma.—There can be no doubt that trachoma is contagious, a fact which was proved by Piringer; the organism, however, has as yet escaped demonstration.

Hirschberg and Krause (1881) obtained bacilli from "acute" trachoma, but failed to find them in chronic cases. Koch (1883) regarded the bacillus now known as the Koch-Weeks bacillus as a concomitant cause with the gonococcus, but erroneously.

Sattler (1881) described a diplococcus as the cause. It resembled the gonococcus, but was smaller. Other diplococci have been described by v. Michel, Schmidt, Kucharski, Raehlmann, Poncet, Staderini, etc. In most cases they stained by Gram's method, and in many inoculation was successful. None, however, have withstood the test of criticism.

Shongolowicz (1890) found a bacillus of extremely slow growth, which gave positive results when inoculated into animals. L. Müller (1897) described a bacillus similar to the influenza bacillus, but difficult to distinguish from the Koch-Weeks bacillus. Morphologically and by culture the differences are minimal, and most critics will agree with Axenfeld in considering them identical.

Little more than an enumeration of some of the wilder flights of

other investigators need be given. Noiszewski found a microsporon similar to the Microsporon furfur (Kaposi) of pityriasis versicolor. Cazalis found the *Streptothrix Foersteri*. Burchardt confounded goblet-cells with coccidia, as did also Ridley, though more guardedly. Elze wrote a treatise on plasmodia in trachoma, and described sixty-two evolution forms.

More interesting are the observations of Krüdener. The presence of pigment granules in trachoma follicles has long been known. In 1881 Leber stated that he had observed swarming movements—like those of swarm-spores—in the superficial cells of fresh trachoma tissue. Krüdener observed the pigment granules under an oil immersion, and also saw movements like those of ciliated epithelium. He called the granules swarm-cells ("Wimmelzellen"). It is suggestive that the granules or cells are commonest when there is a large amount of disintegration products. The appearances are probably due to Brownian movements.

The failure to find a specific organism has led some observers to doubt the existence of any (Mutermilch, Cuénod, Gunning); others have thought that many organisms can cause the disease in predisposed individuals (Cazalis); whilst others have had recourse to a last resource —mixed infection (Lawson and others).

PIRINGER.—Die Blennorrhöe am Menschenauge, Graz, 1840. HIRSCHBERG AND KRAUSE. —C. f. A., v, 1881. KOCH.—Wiener med. Woch., 1883. SATTLER.—B. d. o. G., 1881, 1882. v. MICHEL.—A. f. A., xvi, 1886; Der Mikroorg. d. sog. ägyp. Augenentzündung, Wiesbaden, 1887. SCHMIDT.—Dissert., St. Petersburg, 1887. KUCHARSKI.—C. f. A., xi, 1887. STADERINI.—Ann. di Ott., xvi, 1887. SHONGOLOWICZ.—St. Petersb. med. Woch., 1890. L. MÜLLER.—Wiener klin. Woch., 1897; A. f. A., xl, 1899; A. f. O., lvii, 1, 1903. NOISZEWSKI.—C. f. A., xv, 1891. CAZALIS.—Thèse, Montpellier, 1895. BURCHARDT.—C. f. A., xxi, 1897. RIDLEY.—T. O. S., xiv, 1894. ELZE.—Plasmodienbefunde bei Trachom, Zwickau, 1897. LEBER.—B. d. o. G., 1881. KRÜDENER.—St. Petersb. med. Woch., 1895. LAWSON.—R. L. O. H. Rep., xiv, 3, 1897.

FOLLICULAR CONJUNCTIVITIS

We have stated that follicular conjunctivitis is regarded by some as a precursor of trachoma, the two diseases being in reality one. This position cannot be maintained. It is true that microscopically the follicle and the early trachoma granulation are essentially identical, so that there is little to add as to the histology (Figs. 36, 37). Mayou finds fewer plasma-cells in the subepithelial tissue in follicular conjunctivitis; these are present, on the other hand, in the follicles, whilst they are absent here in trachoma. The discharge contains fewer plasma-cells than in trachoma. Whilst the latter is always accompanied by diffuse inflammation and infiltration, these are often absent in the former. It is therefore not, properly speaking, a conjunctivitis, but merely a symptom indicative of many diverse conditions.

Follicles are normally present in many animals, and may be best demonstrated by treatment with 0·5 per cent. HCl, followed by alum carmin (Leber). This treatment fails to show them in the normal human conjunctiva.

They are frequently found in school children, especially weakly ones, suffering from anæmia, tubercle, etc.; they are also often

associated with hypermetropia. Many of the children affected also suffer from adenoid vegetations in the throat, a pathologically allied

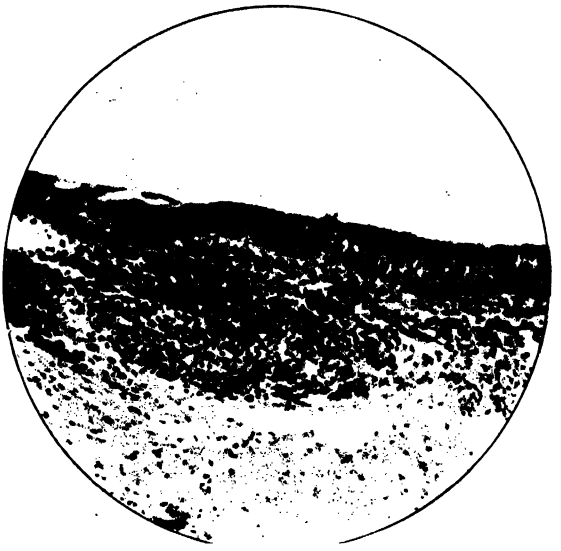


FIG. 36.—FOLLICULAR CONJUNCTIVITIS. × 120.
From a specimen by Herbert.

condition. They occur in many institutions, asylums, etc., and in those living under bad hygienic conditions. Noxious matter in the air, and very various thermal, chemical, and bacterial irritants all



FIG. 37.—FOLLICULAR CONJUNCTIVITIS.
Herbert, T. O. S., xix. Spreading margin of a follicle, showing columns of cells grouped in lymph spaces. C. Epithelium. B. Layers of large plasma-cells. A. The cells of the follicle slightly out of focus; they should be closely packed.

seem able to cause their development. They are familiar in cases of atropine irritation, less commonly with eserine, and rarely with zinc

lotions; rarely also in cases of syphilis and tuberculosis of the conjunctiva.

On the other hand, they never develop as the result of gonorrhœal or diphtherial conjunctivitis, nor after simple chronic catarrh, even if prolonged.

The facts that there may be no conjunctivitis, that the follicles disappear without cicatrisation, and that they occur in districts in which trachoma is unknown, would seem to be fatal to the unitarian theory.

Phlyctenular Conjunctivitis

Phlyctenular or eczematous conjunctivitis has not been fully investigated histologically, owing to the difficulty of obtaining material. Excised phlyctenules show little but intensely inflamed and infiltrated

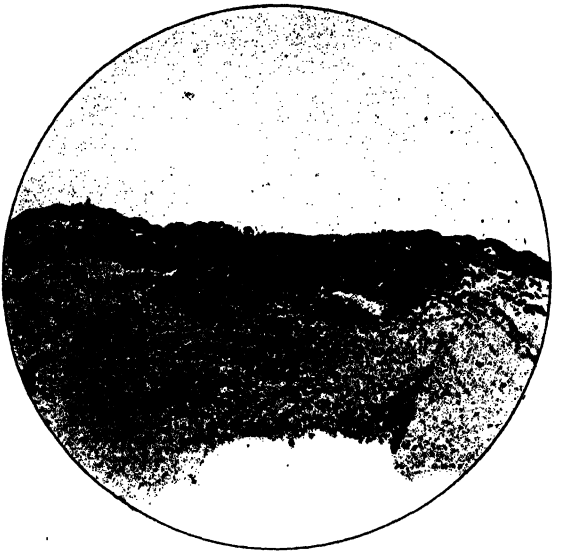


Fig. 38.—Conjunctivitis. × 60.

The specimen was taken from a typical case of episcleritis in an elderly woman. It cannot be regarded as typical pathologically, but resembles the condition found in phlyctenular conjunctivitis. There is a conical area of round-celled infiltration, which also involves the epithelium, though there is no actual ulceration.

conjunctiva, with or without ulceration and loss of epithelium (*cf.* Fig. 38).

Iwanoff (1869) first investigated the subject, and his classical description and figures are familiar from the ordinary text-books. More recently the subject has received attention from Leber, Wintersteiner, v. Michel, etc. (*see also* "Phlyctenular Keratitis").

Leber and Wintersteiner invariably found nodules of round-celled infiltration. The epithelium is raised, then thinned, and finally broken

on the surface. The infiltrating cells are principally polymorphonuclear leucocytes, which are small at the periphery, larger towards the centre, and flattened near the surface, where the nuclei are smaller and stain badly, probably owing to commencing necrosis. Leber found giant-cells in three cases out of four, not always in the nodules, but also under the epithelium. Wintersteiner found them only at the periphery of ulcers. There is never caseation, and the appearances, though they offer some similarity to tubercles, are not identical. The endothelium of the vessels is swollen, shows mitoses, and may be fused into giant-cells.

v. Michel describes the formation of vesicles and pustules, which have not been observed by others. In the first stage there is infiltration with uni- and multi-nuclear leucocytes, which invade the intact epithelium. The lymphatics are dilated, and the blood-vessels full of corpuscles and surrounded by a zone of lymphocytes; thromboses and hæmorrhages may occur. Later, the surface necroses and an ulcer is formed; or the epithelial layers become separated by a fibrinous exudate containing leucocytes and swollen epithelial cells, and minute vesicles are formed. The subepithelial tissues are also œdematous, and contain fibrinous coagulum. An ulcer is also formed eventually, the floor of which is covered with granulation tissue. Healing takes place after the casting off of the necrosed cells by the formation of layers of closely packed spindle-shaped cells, which are covered by epithelium growing in from the edges.

The term "phlyctenule" is only justified if vesicles are formed, as held by v. Michel. It may, however, be retained until accurate knowledge of the pathology and pathological anatomy of the disease is obtained. When vesicles definitely occur, as in herpes, the walls fall together after they burst; whereas a phlyctenule is always solid, and forms a crateriform ulcer (Sattler). The term "eczema" is equally open to objection, since the condition is essentially a scrofulous one (Axenfeld), and the accompanying eczema of the lids is secondary; moreover there is no uniformity as to the pathology of eczema.

Iwanoff.—B. d. o. G., 1869. v. Michel.—Z. f. A., iv, 1900. Leber, Wintersteiner. —B. d. o. G., 1901. Axenfeld, Leber, Wagenmann, Sattler, etc.—B. d. o. G., 1897.

Bacteriology.—Gifford (1886) first investigated phlyctenular conjunctivitis for bacteria; he found *Staphylococcus pyogenes albus* and *aureus* in twenty-six cases out of twenty-eight. Burchardt (1887) found *Micrococcus flavus desidens* (Flügge), and produced phlyctenule-like infiltrations in rabbits' corneæ with it. In a later work (1893) he obtained staphylococci most frequently; often they could be demonstrated only by culture. Leber (1888) failed to produce phlyctenules in man by staphylococci; Burchardt's experiments on rabbits prove nothing. Most later observers have found staphylococci (Gallenga, Morax, Straub, Bach), which may be accessory, though not causal, but are more likely to be mere contaminations.

The observations of Baas (*v.* "Phlyctenular Keratitis") tend to show that the stimulus to the formation of phlyctenules is endogenous and not ectogenous. Leber (1901) was unable to find tubercle bacilli, and

he showed that the skin affection can be induced by cocci cultivated from the eye without skin abrasion, whilst the same cocci are inactive in the conjunctiva even after abrasion of the epithelium. It is possible that the conjunctivitis is due to the action of tubercle toxins. Leber has observed the effects of the injection of sterilised dead tubercle bacilli into the cornea. The bacilli were rapidly taken up by leucocytes. When the injection was made in the centre of the cornea a dense cellular infiltration of the wound, with a greyish zone around it, was the result. This was followed by a small loss of substance, which was gradually restored with more or less vascularisation. Recovery, however, was followed by fresh outbreaks of inflammation and punctiform projecting infiltrates. Experiments with sterilised bacilli injected into the blood-vessels were unsuccessful.

GIFFORD.—A. of O., xv, 1886. BURCHARDT.—C. f. A., xi, 1887; Dermatol. Zeitschrift, i, 1893–4. LEBER.—VII internat. Congress zu Heidelberg, 1888; B. d. o. G., 1897, 1901. GALLENGA.—Ateneo medico Parmense, 1889. STRAUB.—A. f. A., xxv, 1892; Nederl. Oogheelkund. Bydragen, 1896. AXENFELD.—Berlin. klin. Woch., 1897; B. d. o. G., 1897. MORAX.—Thèse de Paris, 1899; Ann. d'Oc., cxvii, 1897. BACH.—A. f. O., xli, 1, 1895; Z. f. A., i, 1897; iii, 1898; Vossius' Sammlung, iii, 1, 1899. MEIJERS.—Dissert., Jena, 1898. HERTEL.—A. f. O., xlvi, 3, 1898. SCHOLZ.—Deutsche med. Woch., 1900; Deutsche Klinik, 1903.

SYPHILIS

Primary chancres occur rarely upon the conjunctiva, especially at the lid margins and the fornix. Hitschmann examined one from the fornix microscopically. He found the epithelium thickened, with "colloid" degeneration in places. Below this was a slightly infiltrated zone of connective tissue, followed by a densely infiltrated part. The infiltration followed the vessels, and consisted of round-cells with a few mast-cells. The vessels were thickened and compressed. Nothing very characteristic was made out, and the case is open to doubt on diagnostic grounds. Gummata also occur.

Syphilitic inflammations tend to show more degenerative changes and necrosis than other types; this is due to the more marked endo- and peri-vascular changes which are found; there is also more proliferation of granulation tissue than usual.

Reiner, Elschnig, and Fialho found diffuse changes in the conjunctiva in their cases. They are probably allied to those found in annular scleritis (q. v.). There were the usual signs of inflammation, with polymorphonuclear cells, plasma-cells, and mast-cells. There were no giant-cells or necrosis. In Fialho's case there were extensive changes in other parts of the eye, with giant-cells.

There are some cases of conjunctivitis with localised redness and swelling in which typical giant-cell systems are found, such as are usually associated with tubercle. Some of these clear up rapidly with mercury and potassium iodide. One such is described fully by Peppmüller, and I have seen another almost identical with this. I was unable to find tubercle bacilli, and Peppmüller failed after prolonged search; eventually, however, they were found in his case.

HITSCHMANN.—Wien. klin. Woch., 1897. REINER.—B. z. A., xxiii, 1898. ELSCHNIG.—K. M. f. A., xxxv, 1897. FIALHO.—A. f. O., lii, 3, 1901. PEPPMÜLLER.—A. f. O., xlix, 2, 1899; l, 3, 1900.

TUBERCLE

Tubercle of the conjunctiva is probably not so rare as has been thought (1 in 6000 ophthalmic cases, Hirschberg, 1881; 1 in 30,000, Mules, 1885; 1 in 2700, Eyre, 1900) (Figs. 39—45).

Sattler distinguished four groups of cases, which have been modified by Eyre as follows:

1. Characterised by the presence of one or more small miliary ulcers, which usually caseate, and may or may not coalesce; these generally attack the palpebral in preference to the bulbar conjunctiva.

Scrapings from these ulcers used to prepare cover-glass films, and suitably stained, say by the Ziehl-Neelsen method, generally show numerous small groups or bunches of bacilli indistinguishable morphologically in their tinctorial reactions from the tubercle bacillus.

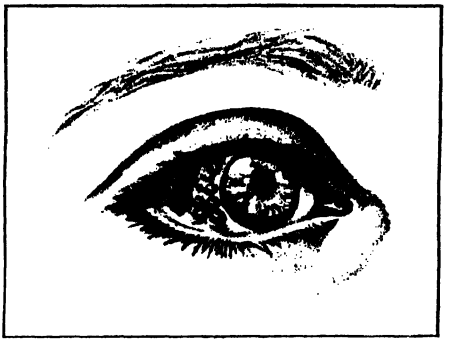


FIG. 39.—TUBERCLE OF THE CONJUNCTIVA.

After Eyre, T. O. S., xvii, pl. i. Case 1, Group 1: showing granulations on the temporal side of the bulbar conjunctiva, with central caseous mass.

2. Characterised by the presence of greyish or yellowish subconjunctival nodules, varying in size, but rarely larger than a hemp-seed—resembling somewhat the sago granules of acute trachoma when grey, or the tubercles met with in the lungs of acute miliary tuberculosis when yellow. These are regarded by Eyre as the initial stage of the next type; these small tubercles, increasing in size by proliferation of the small round-celled exudation which encircles the giant-cell systems, absorb their conjunctival covering. The continued action of the central irritant is responded to by a like activity of the cell elements, and as the growth tends to take place along the lines of least resistance, the fungating granulations of the third group are the inevitable result.

Sections of the small miliary tubercles show well-defined giant-cell systems (Fig. 43); and scattered here and there, without any definite arrangement or relationship to these giant-cells, small groups of tubercle bacilli, seldom numbering more than ten to twelve individuals, can usually be demonstrated.

3. Characterised by the presence of florid hypertrophied papillæ and rounded, flattened outgrowths of granulation tissue, sometimes derived from the tarsal conjunctiva, but usually springing from the fornices (resembling in many respects the velvety granulations met

with in tubercular arthritis), and associated with œdema and thickening of the lids.

Sections of the hypertrophied papillæ and flattened granulations as a rule show nothing but masses of small round-cells with occasional large polygonal cells, but no definite giant-cell systems. Tubercle bacilli are usually scattered, but very sparsely, throughout the tissue, and it generally happens that they are missed. In any case one must be prepared to examine scores of sections, and even then have to record a negative result.



FIG. 40.—TUBERCLE OF THE CONJUNCTIVA.

After Eyre. Case 3, Group II: showing subconjunctival nodules on the palpebral conjunctiva. The lid has been everted.

4. Characterised by the presence of numerous pedunculated *cocks-comb* excrescences on the fornices, of a jelly-like consistence, and often showing more or less superficial ulceration.

Sections of the jelly-like masses occurring in this group consist of masses of small round-cells, but show in addition a large proportion of newly formed blood-vessels of the embryonic type. It is difficult to demonstrate the tubercle bacillus in the sections.

5. Characterised by the presence of a distinctly pedunculated tumour (very rarely more than one may be present), having the macroscopic appearances of a papilloma or fibroma of the tarsal conjunctiva.

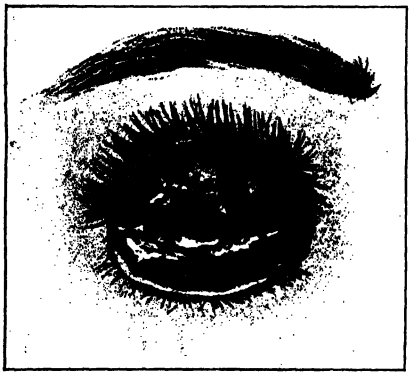


FIG. 41.—TUBERCLE OF THE CONJUNCTIVA.

After Eyre. Case 4, Group III: showing prominent granulations. Both lids have been everted.

Sections of the tumour generally show a stroma of fairly dense connective tissue enclosing a mass of round-cells, with here and there giant-cell systems; and in these systems, or in close proximity to them, tubercle bacilli may be found, either isolated or in small bunches of five to ten individuals.

The first three groups agree in the main with Sattler's; his fourth group is *lupus*, characterised by ulcers with steep swollen edges surrounded by very vascular granulation tissue. Other cases have been described in which there was extensive cicatrisation and shrinking, suggestive of pemphigus (Burnett, Reimar).

The characteristic features described by Sattler and Eyre are sometimes mixed up, so that no hard and fast line can be drawn between the groups. Thus I have seen a typical "cockscomb" excrescence

along the whole lower fornix in which there were crowds of well-defined giant-cell systems. Bacilli are often few and far between in the sections, and demonstration of them is a laborious process. The only absolutely reliable test is inoculation into a rabbit's anterior chamber, which is followed in a few weeks by tubercular nodules upon the iris, and commonly general dissemination and death.

Birch-Hirschfeld carefully examined three cases belonging to Sattler's first, second, and fourth (lupus) groups. The trachoma-like case is interesting in that there is reason to think that it was derived from a cow which was subsequently proved to have "Perlsucht;" if so, this is proof of the identity of human and bovine tubercle, as against Koch's theory. Many cases of this group are undoubtedly treated as trachoma, their true ætiology never being recognised. The lupous cases are doubtless due to transference of infection, lupus of the face, nose, or larynx being usual concomitants (Rhein, Bach, Denig, Grunert, Birch-Hirschfeld). Pannus of the cornea may occur in several of the groups, and adds much to the difficulty of diagnosis in the trachoma-like cases. Uhthoff has recorded a case of the second group following tuberculosis of the lacrymal sac.

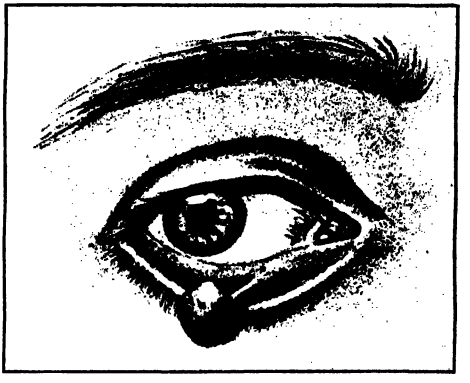


FIG. 42.—TUBERCLE OF THE CONJUNCTIVA.

After Eyre, Case 7, Group V: showing polypoid tumour springing from the conjunctiva of the lower lid.

Zimmermann has published a typical case of Eyre's fifth group, in which an apparently simple polypus, with a long pedicle, was made up of tubercular tissue and contained bacilli.

The reason why tubercle should assume such protean forms in the conjunctiva is probably the very variable virulence of the tubercle bacillus, and also the condition of the individual and the local disposition of the conjunctiva. The first factor is proved by the great differences obtained in inoculation experiments. Valude's experiments have shown that injury of the conjunctiva greatly increases the risk of infection, and these results are supported by Fuchs. Doubtless phlyctenular ophthalmia may run a normal course in eyes previously affected with tuberculosis (Birch-Hirschfeld).

The question whether the conjunctival affection is primary or secondary is difficult to answer in many cases. In the lupous cases it is doubtless usually secondary, but in many of the other cases reported the patients have been quite healthy, or at any rate suffering from no demonstrable tubercular affection. Eyre regards the cases of his Groups I, II, and V as invariably primary. Benson's and Griffith's cases of "primary" lupus were recorded before accurate classification was adopted.

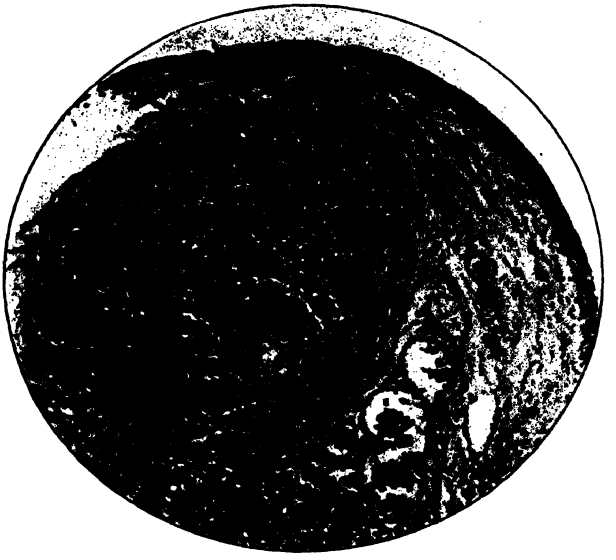


FIG. 43.—TUBERCLE OF THE CONJUNCTIVA. × 120.

From an adult. The whole of the inner and upper parts of the conjunctiva were swollen and congested. No bacilli were found. The condition improved on general treatment with mercury and potassium iodide. The section shows a typical giant-cell system, the group of Langhans' giant-cells being surrounded by an inner zone of epithelioid cells and an outer zone of lymphocytes.

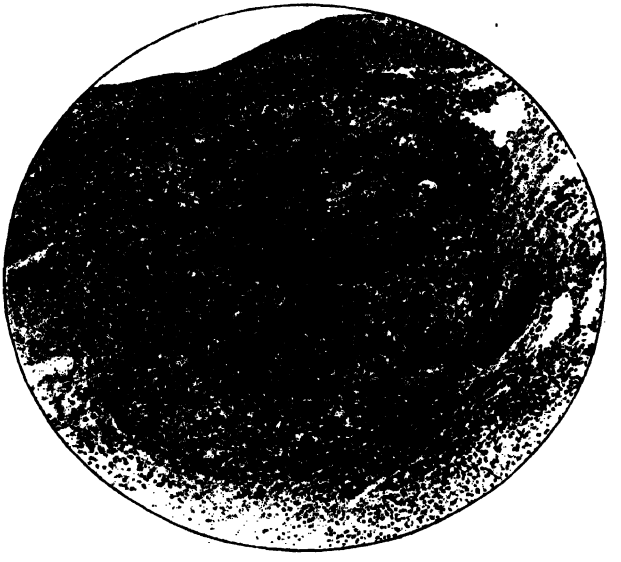


FIG. 44.—TUBERCLE OF THE CONJUNCTIVA. × 75.

The diagnosis is not certain in this case. It is probably a tubercle undergoing involution. From a girl æt. 8. Ocular condition of twelve months' duration, starting simultaneously with cervical adenitis. Mother, brother, and sister died of tubercle. R. eye: chain of four nodules in lower fornix, outermost breaking down. L. eye: marginal phlyctenule below. The nodule consists of epithelioid cells, surrounded and infiltrated with lymphocytes and a few polymorphonuclear leucocytes. The fibrous tissue at the periphery is increased.

Eyre and others have stated that the disease shows no spontaneous tendency to recovery. At the same time Horner, Fuchs, Reimar, and others, including Eyre himself, have obtained good results by mild treatment, *e. g.* iodoform. Nearly all authors, however, agree that radical treatment by knife and cautery is indicated in order to prevent general tuberculosis. The relative virulence of the bacilli and the reaction of the patient's tissues are very variable factors, and where the former is weak and the latter strong, as exemplified by energetic proliferation, the better is the prognosis, and that in greatest degree when bacilli are difficult to find and inoculation experiments have a long incubation period.

The pre-auricular gland of the same side as the affected eye is

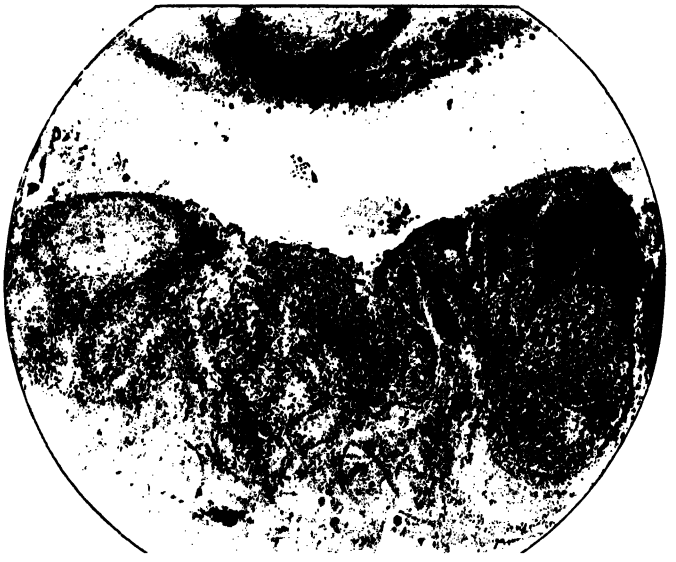


FIG. 45.—TUBERCLE OF THE CONJUNCTIVA. × 55.

From a specimen by Stock (Freiburg-i.-B.). The black patches are due to dirt, the specimen having been removed post mortem. On the extreme left is a typical giant-cell system; on the extreme right below is a typical follicle. The combination is unusual.

usually infected early, and then the next glands in the series, viz. those below the angle of the jaw. This symptom is not infrequently absent, and is only of diagnostic importance when present.

Proof of general dissemination from a primary conjunctival lesion is yet wanting.

*EYRE.—T. O. S., xvii, 1897 (with Bibliography); A. of O., xxix, 1900. SATTLER.—B. d. o. G., 1891. KNAPP.—A. of O., xix, 1890. *BURNETT.—A. of O., xix, 1890. VALUDE, FUCHS.—B. d. o. G., 1887. BACH.—A. f. A., xxviii, 1894. DENIG.—A. f. A., xxxi, 1895. CHENEY.—T. Amer. O. S., 1896. GRUNERT.—A. f. A., xxxiv, 1897. HEINERSDORF.—K. M. f. A., xxxv, 1898. *BIRCH-HIRSCHFELD.—K. M. f. A., xxxvii, 1900 (Bibliography). REIMAR.—K. M. f. A., xxxvii, 1900. CARGILL, JESSOP.—T. O. S., xx, 1900. UHTHOFF.—Berliner klin. Woch., 1900. STOCK.—K. M. f. A., xli, Beilageheft, 1903.

Leprosy

The conjunctiva is most commonly affected by continuity at the lid margins, and after this most frequently at the limbus.

In the C. tarsi there is papillary hypertrophy, consisting of typical leprous granulations covered by flattened epithelium, which is often horny. There are no cylindrical cells. The Meibomian glands rarely show degeneration, though they may be surrounded by crowds of bacilli, and invaded by a few.

At the limbus there are the usual granulations, which seldom extend into the sclera until late in the disease. They cannot be distinguished as leprous from their external appearances, but only by the clinical condition, leprosy of the eye being always a secondary invasion, and by the demonstration of the bacilli.

(For Bibliography, *see* "Lids," "Cornea.")

Ophthalmia Nodosa.

The essential feature of ophthalmia nodosa is a nodular conjunctivitis, not unlike tubercle of the conjunctiva (*pseudo-tubercular conjunctivitis*), but accompanied by acute exacerbations. The first case was brought forward by Pagenstecher (1883), and he was followed by Baas (1888), Weiss (1889), Wagenmann (1890), Krüger (1891-2), Becker (1892), Hillemanns (1894), Lawford (1895), etc.

The condition is caused by the irritation of the hairs of certain species of caterpillar—Lasiocampa or Bombyx (*B. rubi*, *B. pini*), Liparis (*L. monacha*, *L. dispar*), etc. Other species, *e. g.* Cnethocampa (*C. processionea*), also cause conjunctival irritation, but it rarely becomes so severe as with the other species, nor are the deeper parts of the eye (iris, etc.) affected (Baas, Wagenmann). The disease naturally commences only during the period of active life of the caterpillars, viz. August, September, October. One case is said to have occurred in June (Weiss).

The nodules are found in the conjunctiva, episclera, and iris, the favourite situation being the ocular conjunctiva between the lower border of the cornea and the fornix; but they are also found in the palpebral conjunctiva, the retrotarsal folds, and the deeper tissues. They are multiple, varying from three to twenty-six, round or oval, 1 to 2 mm. in diameter, flattened, grey or yellowish, semi-translucent. They are said to be larger in the iris, but these have not been examined microscopically. Their minute structure closely resembles tubercle, but can be distinguished by the presence of the hairs. The hairs act as foreign bodies, but whether the irritation is purely mechanical, due to the serrated contour, or chemical, due to an acid secretion (formic acid [Goossens]) from glands at the base, is uncertain. Probably it is purely mechanical, but the irritation seems to be caused chiefly by the base, and not the apex of the hair. Stargardt considers that the irritation is purely mechanical in the first stage, but that later it is due to

chemical irritation, and it is then that the pseudo-tubercles are formed. The chief constituent of the hairs is chitin (glucosamine-acetyl-acetic acid, Schmiedeberg), and this can split up into glucose and aromatic products.

Microscopically the hairs are found embedded in the conjunctiva, and surrounded by an area of dense round-celled infiltration. Peripherally there are usually numerous giant-cells amongst the round-cells, and still more peripherally simple lymphocytic infiltration (Hanke) (Fig. 46). The giant-cells may be absent rarely. With hæmatoxylin and eosin staining, the section of the hair has a dark brown central axis, surrounded by a strongly refracting yellow zone (Wagenmann, Hanke). The round-cells are ordinary lymphocytes with deeply



FIG. 46.—OPHTHALMIA NODOSA. × 200.
The caterpillar hair is not seen in this section. There is a giant-cell of the Langhans type, surrounded by epithelioid cells and round-celled infiltration.

staining nuclei and scanty cytoplasm. The giant-cells are typical "foreign-body giant-cells," with enormous cell bodies and very numerous nuclei, which may be arranged either centrally or peripherally, as in the Langhans giant-cell. Epithelioid cells, with large, faintly stained oval nuclei and granular cytoplasm, are numerous in the vicinity of the giant-cells. There are also spindle-shaped cells, the whole showing a tendency to concentric lamination around the hair. The structure is well depicted in Krüger's plate.

In one of Krüger's cases the nodules were surrounded by a thick fibrous-tissue capsule, due probably to the prolonged irritation, and the round-cells were degenerated, the nuclei staining badly. The nodules shrink and ultimately disappear if left alone, but scarring may lead to permanent deformity—most serious in the case of the iris.

The superficial epithelium is normal, or somewhat thickened (Wagenmann). The conjunctival stroma is œdematous or sclerosed, the vessels being congested and surrounded by a zone of lymphocytic infiltration, or having sclerosed walls (Hanke, Wagenmann). These differences are doubtless due to the duration of the complaint.

The hairs are usually extremely fine, covered with imbricated cells. These in *Cnethocampa processionea* are arranged in the form of a screw, and have short points (Lord Walsingham in Lawford's paper). The apex of the hair is very sharp, and the base tapers, but the hair is often fractured. Owing to the imbrication it seems probable that the hair travels base forward, its progress being effected by the movements of the eyes and lids, and the rubbing of the eyes induced by the irritation. That the hairs can travel far in the course of time is rendered probable by the case reported by Reis, where a hair was almost certainly visible in the choroid ophthalmoscopically. There seems to be no sufficient ground for Wagenmann's suggestion of definite chemical irritation, but the point is not decided. The secretion of the basal glands is said to pass into the empty hair-shaft (H. Karsten, Leydig, Goossens, C. Keller). Hanke eliminated the question of subsidiary bacterial infection; there were no tubercle bacilli by Ziehl-Neelsen stain, nor, indeed, any micro-organisms by Löffler's method.

Experiments on animals by Krüger and Störmann have led to no very definite results. Conjunctivitis was set up, but no nodules were produced, and the hairs never reached the iris. It is said that drying the hairs renders them innocuous, but this requires confirmation. Further experiments have been made by Stargardt.

Hanke suggests that the nodules are due to "embolism of the smallest capillaries . . . due to the hairs"—not a very probable hypothesis.

PAGENSTECHER.—K. M. f. A., xxi, 1883. BAAS.—K. M. f. A., xxvi, 1888. WEISS.—A. f. A., xx, 1889. WAGENMANN.—A. f. O., xxxvi, 1, 1890. KRÜGER.—A. f. A., xxiv, xxv, 1892; A. of O., xxii, 1893 (tr.). BECKER.—Berl. klin. Woch., 1892. HILLEMANNS.—Deut. med. Woch., 1894. STÖRMANN.—Dissert., Berlin, 1894. LAWFORD.—T. O. S., xv, 1895. ELSCHNIG.—K. M. f. A., xxxiii, 1895. NATHANSON.—K. M. f. A., xxxv, 1897. VOSSIUS.—Z. f. prak. Aerzte, 1897. HANKE.—B. z. A., xxiii, 1898. GOOSSENS.—Ann. de la Soc. Ent. franç., 1881, 1886. LEYDIG.—Arch. f. Anat. u. Phys., 1856. C. KELLER.—Kosmos, xiii. REIS.—A. f. A., xlvi, 1902. * STARGARDT.—A. f. O., lv, 3, 1903.

SPRING CATARRH.

Spring catarrh was isolated as a disease *sui generis* by Saemisch. Cases had previously been described as *conjunctivitis lymphatica* by Arlt (1846), *perikeratic hypertrophy* by Desmarres, *gelatinous thickening of the limbus* by v. Graefe, *phlyctæna pallida* by Hirschberg. It was called *conjunctivitis verrucosa* by Goldzieher.

Spring catarrh occurs in two situations—as flat-topped papules, resembling cobble-stone pavement, on the C. tarsi of the upper lid, and as a gelatinous or fleshy hypertrophy of the C. bulbi at the limbus. The two forms are found separately or combined, and may be so slight that there is only conjunctival injection with minimal thickening. Other parts of the conjunctiva are normal.

The palpebral papillæ are large, flat-topped, and polygonal by mutual pressure; they are often of cartilaginous consistence. They may be several millimetres in diameter, and are often broader than they are high. They have a milky white shimmer, which is also seen over

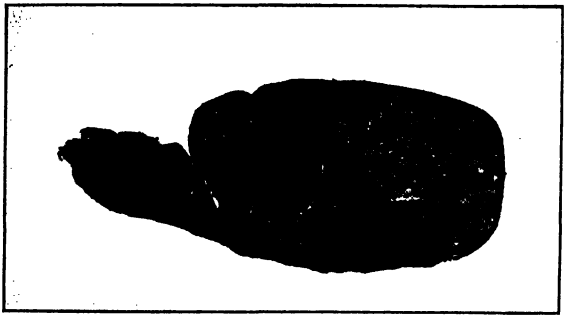


FIG. 47.—SPRING CATARRH. × 34.

From a specimen by Herbert. A palpebral papilla cut vertically. Note the shape, and the thinning off of the epithelium on the surface to the left. The papilla contained many eosinophile corpuscles.

the lower tarsus, where there is merely thickening without papillary formation. In vertical section the papillæ have the shape of the circumvallate papillæ of the tongue (Fig. 47). In Spicer's case the pedicle was unusually slender. They consist of a mass of dense, often hyaline, fibrous tissue, with comparatively few round and spindle-shaped cells, and scattered blood-vessels. The epithelium covering them is thickened from the normal double layer to five or more layers, and this is the cause of the milky appearance. There are often true



FIG. 48.—SPRING CATARRH.

Herbert, T. O. S., xix. A palpebral papilla, showing very extensive epithelial downgrowth, both in long branching tubules and shorter irregular solid cords.

papillæ on the surface, and epithelial plugs may descend for some distance into the stroma (Fig. 48). The growths are rather of the nature of fibromata than papillomata (Spicer).

The hyperplasia at the limbus was observed earlier, and has been

investigated more fully than the palpebral condition. The nodular growths are found chiefly at the outer and inner sides of the cornea, which they invade for a short distance. They extend farther into the

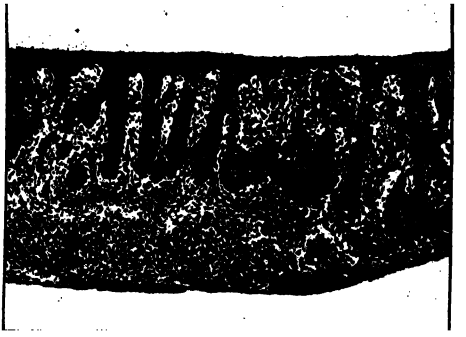


FIG. 49.—SPRING CATARRH. × 60.

From a specimen by Herbert. From the limbus, showing downgrowths of epithelium.

conjunctiva, and may surround the cornea with a wall of gelatinous tissue. They are sharply limited on the side of the cornea, in which there is often a grey stria, separated by a zone of clear cornea, like an arcus senilis. The nodules never ulcerate. Their structure is essen-



FIG. 50.—SPRING CATARRH. × 120.

From a specimen by Herbert. From the limbus, near a spot which stained with fluorescein, showing mode of absorption of epithelial downgrowths, eruption of eosinophiles, etc.

tially the same as that of the papillæ, but the epithelial thickening has been more often remarked than the fibrous undergrowth, possibly owing to incomplete removal. The epithelium is usually three times the normal thickness, having thirty to forty layers of cells. The normal

papillæ in this situation are accentuated and multiplied, and epithelial plugs often extend deeply into the tissues (Vetsch, Horner) (Fig. 49). These often show nests and resemble epithelioma, but the basement membrane is always intact. The superficial cells are flattened and may have lost their nuclei, but actual cornification has not been observed. Reymond first pointed out the fibrous hyperplasia as the essential feature; Knus found it occupy only one third of the section, whilst in Burckhardt's case it was much thicker than the epithelium. It consists of looser fibrous tissue with more cells. These are of three kinds: (1) small spindle-cells, deeply stained, which are ordinary connective-tissue cells; (2) large clear oval cells, often with karyomitoses—these are probably embryonic connective-tissue cells; (3) small round-cells, deeply stained, which are infiltrating lymphocytes. As the condition progresses the fibrous tissue becomes less cellular, and firmer and more compact (Schlub). The cells and the connective tissue often show peculiar hyaline degeneration in the later stages.

Schiele found enormous thickening of the epithelium with club-shaped downgrowths in a case of bulbar vernal catarrh. With iodine solution the superficial cells stained mahogany red, the deeper ones wine red; infiltrating cells and connective-tissue cells stained diffusely. Schiele deduces the presence of glycogen in these situations.

Danvers found numerous mast-cells and plasma-cells in one case San Felice's method of staining blastomycetes failed to reveal any; no bacilli were found by Gram's stain.

Herbert describes eosinophile infiltration of the tissues, and the presence of minute vesicles in the epithelial layers of the pedunculated growths, which are also filled with the eosinophile cells (Fig. 50). He further noted that in the blood there was an increase of 10 to 20 per cent. in the eosinophile count; this may, however, have been due to other causes, though it was not found in other conjunctival conditions. The secretion obtained by exposing the conjunctiva for a short time also contains many eosinophiles.

The nodules do not seem to alter much during the quiescent winter period, but they probably become more infiltrated and cellular in the summer.

SAEMISCH.—In G.-S., iv, 1876. REYMOND.—Ann. di Ott., iv, 1874. VETSCH.—Inaug. Diss., Zurich, 1879. UHTHOFF.—A. f. O., xxix, 3, 1883. EMMERT.—C. f. A., xii, 1888. HORNER.—In Gerhardt's Handb. d. Kinderkrankheiten, v. Tübingen, 1889. KNUS.—Inaug. Diss., Zurich, 1889. SCHOEBL.—C. f. A., xiv, 1890. TAILOR.—Ann. di Ott., xx, 1891. BURCKHARDT.—Inaug. Diss., Basel, 1894. *SCHLUB.—A. f. A., xxxv, 1897. NATHANSON.—K. M. f. A., xxxviii, 1900. AHLSTRÖM.—K. M. f. A., xxxviii, 1900. HOLMES-SPICER.—T. O. S., xx, 1900. SCHIELE.—A. f. A., xix, 1889. DANVERS.—Spring Catarrh of the Eyes, London, 1901. *HERBERT.—Brit. Med. Jl., 1903.

PEMPHIGUS.

One of the earliest cases of pemphigus of the conjunctiva was published by White Cooper (1858); before that date—and since also—it has been confused with xerosis. It was described as *syndesmitis degenerativa* by Stellwag (1870), and as *essential shrinking of the con-*

junctiva by Kries (1878), of von Graefe's clinic. von Graefe (1879) propounded the identity of pemphigus and essential shrinking, whilst Becker (1879) admitted only the identity of the latter with syndesmitis. v. Graefe's view is now generally admitted (Fuchs and others).

The condition is rare, 5 in 45,000 (Franke), 2 in 22,000 (Pergens) amongst ophthalmic cases, 0 in 200 (Hebra) amongst cases of pemphigus. Cases may be divided into (1) those with blebs on the skin, (2) those with blebs on the mucous membranes (mouth, nose, larynx, etc.), (3) those with blebs on the conjunctiva only, (4) those with essential shrinking only (Pergens). Of 132 cases collected by Pergens, 9 acute and 68 chronic belong to the first group, 15 to the second, 2 to the third, and 16 to the fourth; in the remainder the ætiology is doubtful. The majority of the patients were adults, but the ages vary from 1 to 78. The prognosis is bad in all cases watched for a prolonged period; the best result is a case in which the cornea was clear a year after coming under observation (Marcus Gunn).

In the earlier stage blebs occur upon the conjunctiva and cornea, but these are rarely seen. The epithelium here is much more delicate than that of the skin, and as only the epithelium, or even the superficial layers alone, are raised, they are quickly torn and disintegrated. The denuded areas are then seen, and these rapidly become covered by a grey coating, which contrasts with the general reddening of the conjunctiva. As the spots cicatrise, new blebs and ulcers appear in other places. Cicatrisation is accompanied by excessive contraction, resembling that occurring in keloid scars. Slowly but surely the whole conjunctiva becomes opaque, white, and tense; the folds of transition disappear, and bands stretch vertically from the lids to the globe, the lids being finally retracted. The lacrymal ducts become occluded and the conjunctiva becomes dry. The cornea becomes ulcerated, and at last opaque, and eventually total symblepharon results.

The bullæ of pemphigus in the skin occur in various layers of the epithelium, or the whole epithelium may be raised (Radcliffe-Crocker). So it is apparently in the conjunctiva. Franke found that the outer wall consisted of only two or three layers of cells, and did not therefore involve the whole thickness. The fluid contents are at first clear serum; later they invariably become cloudy, and contain fatty degenerated epithelial cells, leucocytes, a few red corpuscles, and granular *débris* and coagulum (Schiess).

Sattler found considerable swelling of the conjunctiva due to enormous œdema, and swelling of the fibrous tissue. There was no lymphoid infiltration, but this is usually present. The whole stroma was pervaded by granular material, which extended over the cornea. The ulcers are rapidly covered by a fibrinous coagulum, so that a pseudo-diphtheritic membrane is produced.

A later stage is described by Uhthoff. The C. tarsi showed a saucer-shaped depression, extending in places deep into the tarsus; it was filled with granulation tissue. The epithelium was absent for the most part, but the edges were covered with a thin, new-formed layer. There was considerable inflammatory infiltration, especially in the upper fornix, with strongly developed papillæ. The epithelium showed

mucous degeneration, and was raised in places, but did not show any typical blebs.

Later still, as in Sachsalber's case, the epithelium is much thickened, and sends coarse plugs down into the subconjunctival tissue. The superficial layers are horny. The adenoid layer is destroyed, and the submucosa is thickly infiltrated with round and spindle-shaped cells. It is highly vascular, and the fibrous tissue is enormously hypertrophied.

Similar changes occur in the cornea, which is transformed into vascular scar tissue, covered by thickened, papillary, horny epithelium (Bäumler). Deutschmann examined the pterygium-like growth which occurs at the edge of the cornea, and found greatly thickened horny epithelium lying on hypertrophied fibrous tissue.

Bacteriology.—The bacteriology of pemphigus of the skin has led to discordant results, and the condition is now regarded as due to the action of toxins upon the nerve centres (Radcliffe-Crocker). This brings the condition into line with herpes, and the conjunctival condition shows many points of similarity with neuro-paralytic keratitis.

It is generally held that the fresh blebs, containing clear fluid, are sterile (Löffler, Uhthoff). Later, when the fluid is turbid, staphylococci (*aureus* and *albus*), streptococci, etc., have frequently been found, but must be looked upon as contaminations which have wandered in from the surface. Xerosis bacilli are present in large numbers upon the surface and in the epithelium, especially in the later stages.

Specific organisms have been described. Plimmer obtained from a case of Silcock's a micrococcus which was apparently identical with that obtained by Demme and Bullock and Wells, from acute pemphigus. It was obtained in pure culture from a bleb on the hand. It usually occurs as a diplococcus, rather larger than the gonococcus; forms round white colonies on agar; grows rapidly in bouillon at 37° C.; well on agar and serum; badly, with slight liquefaction in two or three weeks, on gelatine at 22° C. The cocci stain with all aniline dyes, and by Gram. Injected into the peritoneum of a mouse, they caused death in fourteen hours; into the pleural cavity in forty-eight hours. Inserted into the scarified conjunctival sac of a rabbit, they caused much more rapid suppuration than is produced by other septic organisms.

Deutschmann found a streptococcus which he considered "with some probability" to be specific. Inoculation of a rabbit's ear caused blebs which contained the organism.

White Cooper.—R. L. O. H. Rep., i, 1858. Stellwag.—Lehrbuch d. Augenheilkunde, 6th ed., 1870. Kries.—A. f. O., xxiv, 1, 1878. Radcliffe-Crocker.—Diseases of the Skin, London, 1903. Schiess (-Gemuseus).—Jahresb. d. Augenheilanstalt zu Basel, 1889. Sattler.—B. d. o. G., 1879. Uhthoff.—Berliner klin. Woch., 1893. Sachsalber.—K. M. f. A., xxxii, 1894. Bäumler.—K. M. f. A., xxiii, 1885. Lang, Critchett and Juler.—T. O. S., vi, 1886. Marcus Gunn.—T. O. S., xiii, 1893; xv, 1895. Pernet.—Brit. Med. Jl., 1895; Tr. Derm. Soc., iii, 1897. Pernet and Bullock.—Brit. Jl. of Derm., viii, 1896. Silcock.—T. O. S., xvii, 1897. Deutschmann.—B. z. A., ii, 1891; Münch. med. Woch., 1898. v. Michel.—Z. f. A., iii, 1900. *Franke.—Der Pemphigus u. d. essent. Schrumpfung d. Bindehaut d. Auges, Wiesbaden, 1900. *Pergens.—Pemphigus des Auges, Berlin, 1901.

Conjunctivitis Petrificans.

Conjunctivitis petrificans is a rare disease, first described by Leber in 1895. The full report of his cases is a model of exhaustive investigation. Another case has been reported by Reif.

The conjunctiva is inflamed and covered with opaque white spots or plaques, which project little above the surface, and are not due to exudate, but to an altered condition of the tissue itself. They commence as small round or irregular spots, of chalky whiteness, which gradually extend superficially and in depth, involving more and more of the bulbar and palpebral conjunctiva. The lower part of the scleral conjunctiva and neighbouring part of the fornix seem to be first attacked, but it also commences simultaneously in different parts. New spots apparently arise also by contact infection, and both eyes may be involved. The conjunctivitis is relatively slight. The surface of the larger plaques is uneven and stony hard. The cornea does not usually suffer severely. The affection is chronic, marked by severe exacerbations, but ultimate recovery may ensue.

Microscopically the epithelium is absent in parts, in others irregularly thickened. It may contain calcareous crystals. The stroma shows proliferation of connective tissue, with deposits of calcareous salts. These are partly inorganic salts—carbonates and phosphates,—partly organic, as shown by their solubility in alkalies. The calcified part forms a superficial zone permeated by crystals and fine amorphous particles, which are partly diffuse and partly clumped. On decalcification the substratum is partly homogeneous, partly composed of coarse masses, especially in the deeper areas. The deep zone, below the calcareous zone, consists of fibrous tissue in active proliferation. The fibroblasts are increased in size and number, and the tissue is infiltrated with round-cells. The fibrous bundles are irregularly thickened, and show hyaline degeneration; in places they are infiltrated with fibrinous coagula, and elsewhere are wholly necrotic. The deep vessels show endothelial proliferation; in one case they were blocked by hyaline thrombi, and the walls showed hyaline degeneration. The hyaline material showed every gradation of stain to the fully developed amyloid condition, but the latter was small in amount. The layer between the superficial and deep zones, the "petrification zone," contained sheaves and rosettes of calcareous crystals. Even in parts where no deposits could be seen the tissue contained an excess of lime salts, octahedra of calcium oxalate being deposited on the addition of oxalic acid.

Giant-cells were found in one case in contact with the calcified material; they were the ordinary irritation giant-cells (so-called foreign-body giant-cells). A noteworthy feature was the enormous aggregation of eosinophile leucocytes beneath and within the necrotic part.

In one case all the other features were present without any necrosis.

Leber regards the condition as a parasitic one, though he failed to obtain positive results by staining, culture, or inoculation. The massing of eosinophile cells in the zone of infiltration proves a strong chemo-

tactic action of the necrotic tissue upon the leucocytes in the blood. They appear to break up and set free their granules, dissolving the tissues by their histolytic ferment, so far as the calcification permits. The giant-cells probably have the same function.

The inflammatory proliferation of connective tissue and endothelium is probably the primary event; the vessel walls are injured, and the tissues are flooded with plasma, which forms fibrinous coagula; these degenerate into hyaline and amyloid material, becoming calcified by the copious deposition of lime salts. The necrosis is secondary, caused partly by the blocking of the vessels by degeneration and thrombosis, and partly by the virulence of toxins.

LEBER.—B. d. o. G., 1895. REIF.—A. f. O., l, 1, 1900. *LEBER.—A. f. O., li, 1, 1900.

DEGENERATIONS.

CONCRETIONS.

Concretions are of frequent occurrence in elderly people in the lower fornix, and less frequently in the C. tarsi. They appear, either by the naked eye or with a loupe, as white or yellow specks arranged in horizontal rows or in groups. They are often expressed by slight manipulation; in other cases they are more deeply set. They are the products of degeneration of cells and mucoid exudate in the lumen of minute cysts (*v. infra*).

The cysts are retention cysts of glands of new formation, due to irritation, and also of the so-called Henle's glands. They are surrounded by an area of lymphocytic infiltration. Their walls consist usually of a double layer of epithelium, the inner layer being cubical or cylindrical, with numerous goblet-cells (Fig. 51). The epithelium is usually intact, but may be flattened by the pressure of the concretions, or absent in places from atrophy, or thickened by proliferation. Some of the cells are swollen and degenerated, others are cast off into the lumen and help to form the basis of the concretions (Wintersteiner). They, however, play a relatively small part, and their co-operation could not be proved by Fuchs. Both authors agree in their descriptions of the concretions, and their conclusions can easily be confirmed by anyone.

Each space contains one to five concretions—usually one only,—but all are built up by aggregation. They are usually hyaline, with faint or well-marked lamination (Fig. 52), best seen at the periphery, though many have radial striations here. Like all these degeneration products, they stain variously according to their chemical constitution. They stain very well with safranin (Wintersteiner), red with eosin, peripherally or in zones with hæmatoxylin, variably with fuchsin, not at all with carmin, yellow with van Gieson, violet in parts with Gram, not at all by Löffler's methylene blue, red with orseille. They do not contain calcium carbonate or phosphate, give no xanthoproteic, murexide, or amyloid reactions (Fuchs). They are stained blue by thionin, faint

brown or violet with vesuvin, faint violet with mucicarmin. They do not, therefore, give mucin reactions. They belong to that indeterminate quantity—v. Recklinghausen's hyalin (*v. infra*). Both dyes and culture experiments fail to show the presence of bacteria, actinomyces (*cf.* orseille), or botryomyces (Fuchs).

Besides a variable amount of inflammatory infiltration in the connective tissue, with occasional mast-cells and nodules of brown pigment, small hyaline globules are often present, as in other conditions, *e. g.* trachoma. They are not of any pathogenic importance.

The stages in the formation of these hyaline bodies have been exhaustively worked out by Fuchs. Numerous polymorphonuclear leucocytes infiltrate the epithelium, and are present, usually much

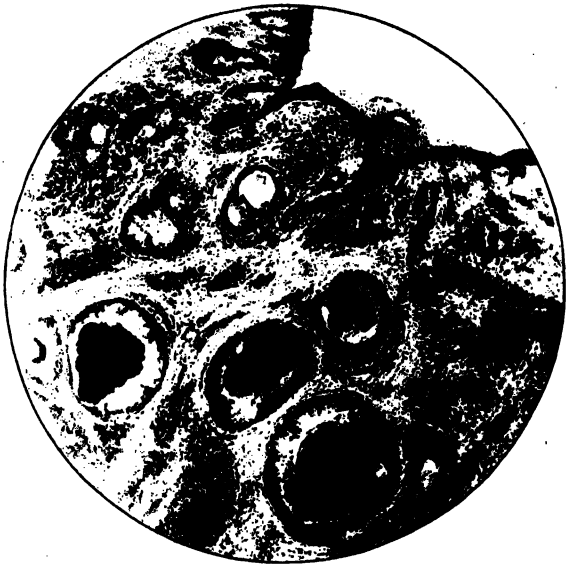


FIG. 51.—CONCRETIONS IN THE CONJUNCTIVA. × 55.

The concretions are contained in new-formed glandular depressions, which are cut across. The walls of the cystic spaces are lined with goblet-cells, many of which have discharged their contents. Some glands are seen which do not contain concretions.

degenerated, in the lumen. Their nuclei often form branching filaments with nodular enlargements amongst the cells, similar to those described by Peters in conjunctivitis (*v.* p. 56). Many lumina are empty; others contain homogeneous or finely granular lumps or networks. Mono- or polymorpho-nuclear cells, or both, are often present, usually bereft of a definite cell body. They are also found in cystic spaces in the epithelium, frequently sickle-shaped with a cell body. Nuclear fragments and clumps occur. Swollen epithelial cells are found in the walls and free in the lumen; the latter swell into granular masses and their nuclei degenerate, or they stain deeply with eosin and retain their nuclei (Wintersteiner).

The smallest concretions seem to be swollen nuclei (Fuchs); these fuse, showing larger bodies with crenate edges. Laminated concretions are found embedded in deeply staining nuclei. Larger, more faintly staining ones with indications of a nucleus are seen. These are probably of epithelial origin. Others fuse into complex, tubularly arranged masses, each tubule having a darker, radially striated cortex. Increase in density occurs both at the periphery and in the nucleus in different cases, and in this manner laminæ may be laid down resembling a renal calculus. The concretions may grow out of the mouth of the gland and project from the surface, or the mouth may be closed by a mass of cells. The smaller bodies are often surrounded by



FIG. 52.—CONCRETIONS IN THE CONJUNCTIVA. × 55.

The concretions are distinctly laminated, and stain variably with hæmatoxylin and eosin. They are contained in glandular cystic spaces in a pigmented nævus of the plica semilunaris removed from an elderly man.

a homogeneous layer of mucoid substance, but in no case do these mucoid deposits give true mucin reactions. In some cases there is a membranous covering, which spans the crenations, and is best seen when raised from the concretion near the mouth of the gland. It resembles an endothelial membrane, and is in places definitely cellular.

Concretions with radial striations of the periphery much resemble actinomycetes, and were erroneously described as such by de Vincentiis in one case, and by Fuchs in his earlier communication to the Ophthalmological Society at Heidelberg. This has been disproved by Fuchs' later researches and by Wintersteiner. Faber published a case as

botryomycosis, similar to the condition found in horses, but this is also probably a mistake.

Antonelli found hyaline concretions in cysts of Krause's glands; in this case he was able to trace the development from blood-clot. Wintersteiner described laminated concretions, exactly similar to the ordinary conjunctival ones, in cysts of Krause's gland; the presence of typical foreign-body giant-cells was peculiar to this case, but might well occur in all cases, and, indeed, indications of their formation are not wanting.

Mitvalski reported similar "colloid pearls" of the Meibomian glands.

ANTONELLI.—Ann. di Ott., xix, 1890. DE VINCENTIIS.—Lav. d. Clin. oc. di Napoli, iii, 1891–3. MITVALSKI.—C. f. A., xxi, 1897. FABER.—38 Jahresb. der Augenheilanstalt in Utrecht, 1897. *FUCHS.—B. d. o. G., 1896; A. f. O., xlvi, 1, 1898. WINTERSTEINER.—A. f. O., xlvi, 2, 1898.

HYALINE, COLLOID, AND AMYLOID DEGENERATION.

Degenerative changes, leading to the formation of homogeneous material, are of frequent occurrence in all parts of the eye, as also elsewhere in the body. The material varies very much in its staining reactions, undoubtedly owing to its variable chemical constitution. It has therefore received various names, such as hyaline, colloid, amyloid, etc., and this has led to great confusion. In all probability these substances are entirely formed from exudates or secretions, *i.e.* from the non-living products of living cells. In some cases this must be considered a physiological process, as, *e.g.*, when Descemet's membrane is laid down by the agency of the endothelial cells, the lens capsule by the epithelial cells, Bruch's membrane by the pigment epithelium of the retina, etc. In others it is a pathological process, which may be allied to the physiological, as in the formation of the so-called "colloid" bodies of the choroid, etc., but is more commonly due to chemical changes in exudates derived from the lymph or blood-plasma. Most of these exudates are proteids, or consist chiefly of proteids. They are inert, dead material, lying amongst living cells, and their subsequent fate depends upon their environment. This, in turn, varies with the general conditions of the organism, as well as with the exact local disposition, such as relationship to vessels, cells, etc. Hence it is not surprising that the changes these exudates undergo differ in widely divergent ways. Some are mere plasmatic coagula, others contain living or dead leucocytes. The first stage is often the formation of a network of fibrin, and this may simply disappear, forming the pabulum of rapidly growing fibroblasts, or melting by ferment action into soluble proteids, which are carried off in the lymph-stream. In less active conditions—marasmic, senile, and so on—the exudates stagnate. They then undergo chemical changes, whereby they slowly alter from substances giving all the proteid reactions to substances which give only "albuminoid" reactions, and these vary much amongst themselves. Some have fairly definite colour reactions; if they stain mahogany-brown with iodine and pink with methyl violet, they are called

amyloid, and this seems to be a fairly stable entity. Often, however, the reaction is indeterminate; parts fail to show the reaction, others show it well, whilst yet others give intermediate tints. We are dealing with mixtures, or with bodies in a state of chemical change. These facts must be carefully borne in mind whenever we speak of hyaline bodies or degeneration, etc. The earlier observers did not always realise them, and it will be necessary to refer to their views; but many of the apparent contradictions are due to these facts, and many of the divergent views are but the expression of divergent processes.[1]

Since the word "hyaline" has not obtained so determinate a significance as "colloid," etc., and is less liable to lead to confusion, it will generally be used throughout the following pages. It must, therefore, be considered to have a very wide significance, and not even so restricted a one as v. Recklinghausen's, which may be termed "hyalin" for distinction.

v. Recklinghausen described a substance which he called "hyalin," and which had the following peculiarities:

1. It was homogeneous and highly refractile.

2. It was extremely resistent to reagents, being insoluble in strong acids and alkalies.

3. It stained deeply with dyes, especially eosin and acid fuchsin, also carmin, picrocarmin, safranin, etc., less and more variably with hæmatoxylin; but it did not give the characteristic amyloid reactions.

Raehlmann first described this substance in the conjunctiva; he found it in adenoid tumours growing from the caruncle and lower fornix. He found it both alone and in conjunction with amyloid tumours, and he regards hyalin as a precursor of amyloid, in which view he is supported by his pupil Kubli. Vossius, on the other hand, in describing two cases of hyaline degeneration of the conjunctiva, distinguishes strongly between hyalin and amyloid. They occurred in young people, free from any constitutional defect, though they had had trachoma. In one case both eyes were affected, in the other only one upper lid. Firm, smooth, pale reddish-yellow tumours grew from the neighbourhood of the fornix; some were furrowed, resembling the cerebral convolutions. They consisted of masses of adenoid tissue with hyaline degeneration, which gave reactions corresponding with v. Recklinghausen's hyalin. The fibrous tissue of the reticulum was irregularly swollen and homogeneous, and in places massed into large irregular nodules; the cells were atrophied by pressure. The larger blood-vessels showed endo- and peri-vasculitis, amounting in many cases to endarteritis obliterans. The thickened walls were hyaline, with a fine concentric lamination, possessing few or no nuclei. The walls of the capillaries were transformed into thick hyaline tubes, with much constricted lumen.

Kamocki has also reported a case.

Both the hyaline and the true amyloid degeneration of the conjunctiva seem to be extremely rare everywhere except in Russia.

[1] *See* PARSONS, Drusen, T. O. S., xxiii, 1903.

v. Oettingen described the first case of amyloid degeneration of the conjunctiva in 1871, and the subject has been well investigated by Raehlmann and Kubli, of the Dorpat Clinic, and by Vossius. The disease usually occurs in people from twenty to thirty-five years old, and is extremely chronic, and incurable. Many cases are associated with trachoma, but this is purely incidental, since it may be circumscribed in an otherwise healthy conjunctiva (Reymond). The patients may also be quite healthy, thus differing from cases of amyloid disease of the intestines, spleen, kidneys, etc. The onset is insidious and the progress slow, but is occasionally rapid. Only one eye is usually affected. It involves particularly the upper fornix and the plica semilunaris, avoiding the more firmly attached parts. Kubli distinguishes four phases: (1) simple adenoid proliferation; (2) hyaline degeneration; (3) amyloid degeneration; (4) calcification and ossification.

The earliest stages are described by Raehlmann. The epithelium is intact; the subepithelial tissue is packed with lymphocytes, the adenoid layer being enormously increased. The structure is that of ordinary lymphoid tissue—a fine reticulum, with nuclei at the nodes and round-cells in the meshes. The latter are degenerated in patches, forming hyaline masses from which the nuclei have disappeared. They are stained by tannate of iron (Raehlmann). The vessels show hyaline degeneration, the walls being transformed into broad homogeneous rings. There is no amyloid reaction in the early stages, but later both hyalin and amyloid and intermediate forms occur simultaneously.

Herbert has described a case of hyaline degeneration of the conjunctiva; he prefers the term "colloid" degeneration, by analogy to similar processes occurring in the skin (Unna). With iodine the substance stained pale brown; with iodine and sulphuric acid, faint indigo blue, "possibly due to cholesterine;" with methyl violet and gentian violet there was no trace of pink coloration.

On account of the application of Unna's methods to the investigation of this case, it merits more than passing notice. Herbert describes his results as follows:

"In most sections the epithelium is found thickened, and this is more by swelling of the cells, which are rounded, than by increase in their number. There are mucus-cells among them, but they are abnormal in retaining the blue colour of polychromic methylene blue on decolourising with glycerine-ether mixture (Fig. 53).

"Below the epithelium is a layer of lymphoid tissue of varying thickness; its occurrence is, of course, quite abnormal in the ocular conjunctiva. The cells are more widely separated than in ordinary adenoid tissue, especially close beneath the epithelium. Lying between them is a quantity of swollen material disposed in ill-defined and irregular lumps, and small fragments and bands, whose origin from normal connective-tissue fibres (collagen) can be traced only with some difficulty, owing to the advanced stage of the process. It requires care to make certain that the swollen, broken-up, and rearranged tissue is not a deposit or infiltration replacing normal collagenous fibres absorbed. This is the very rare change which has been described in

the skin as colloid degeneration.[1] The colloid material has no very striking staining peculiarities; it takes up orceïn well, as does normal collagen. Here and there in the deeper part of this layer is seen enclosure (partial or complete) of the cells in rings of colloid. A few lymphocytes are so closely invested that the appearance is given of colloid transformation of the protoplasm of a cell. The larger cells, plasma-cells, lie loosely within the rings, not in close contact with them. There are a few scattered hyaline balls to be found. This is the true hyaline degeneration which has been exhaustively described[2] in other parts of the body, and is found sparingly in trachoma follicles, in enormous quantity in transverse corneal films, etc. Here and there an unusual yellowish tint is noticeable in some of the spheres stained with acid fuchsin; possibly this colour is derived from the blood which

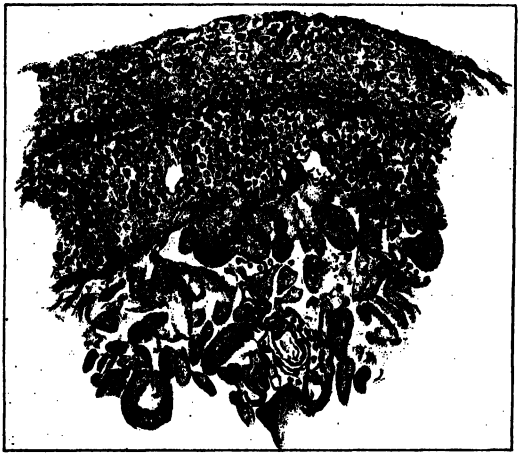


FIG. 53.—"COLLOID" DEGENERATION OF THE CONJUNCTIVA. × 144.

After Herbert, T. O. S., xxii, pl. xix. Stained by acid orceïn, hæmatoxylin, acid fuchsin, and picric acid: showing epithelium above with swollen cells, the deeper tissues infiltrated with leucocytes and containing hyaline masses. Note the deeply stained elastic fibres near dilated blood-vessels.

recently infiltrated the tissue. To the same source is to be attributed the numerous particles of golden-yellow pigment lying among the cells.

"The colloid change is still more developed throughout the deeper tissues, which consist mainly of large, sharply defined, rounded, and elliptical free blocks of colloid. The coalescence and moulding of the material into these masses is probably largely due to constant stretching and movement of the loose conjunctival fold under the working of the upper lid. The centres of many of the blocks stain very feebly, and in many there are definite central cavities. Some of these masses certainly represent sections of the fragmentary remains of blood-vessels, for occasionally more or less definite relics of endothelium and

[1] *See* UNNA, Histopathology of the Diseases of the Skin, London, 1896.
[2] *See* UNNA, loc. cit.

concentric elastic fibres can be made out in them. Others, with large cavities, enclose various contents—in most cases a single plasma-cell, rarely a smaller piece of colloid or a small collection of golden blood-pigment. Here and there the enclosure is incomplete, the two ends of the encircling band of colloid not having yet joined together. These and rarer appearances explain how the cells, etc., become completely surrounded. Embedded in the substance of a few of the blocks—not lying free in spaces—are small spheres, the larger of them having concentric markings, which are usually seen stained exactly like the mass in which they lie, and are recognisable only by a different refractive index. Other blocks without hollow centres are seen, after staining with acid fuchsin, to contain degenerating collagenous fibres, disposed either in a central coil or network, or ramifying throughout the mass. Prolonged staining with acid orceïn shows in a smaller number degenerating elastic fibres similarly embedded; they are of very uneven thickness, some of them separating into fragments. Complete fusion of elastic fibres into a block is occasionally seen by its staining darkly with acid orceïn; the result has been named by Unna 'collastin.' Many of the blocks have connective-tissue cells closely applied to them, following their curves; this corresponds with the former close contact between such cells and the connective-tissue bundles.

"There are still a few bands of white connective tissue (collagen) remaining, which have resisted the early colloid change, and which appear to be degenerating in a direction somewhat apart. They colour abnormally, deeply both with acid fuchsin and acid orceïn; in parts the separate fibrils may be seen swollen and breaking down into droplets and small fragments. Such bands pass obliquely through the tissues, and in parts of most of the sections there is one lying immediately beneath the superficial adenoid layer of conjunctiva. There is very little free elastic tissue remaining; what there is is mostly clumped and coiled in the neighbourhood of blood-vessels. Some of the fibres are swollen, and apparently melting down. Appropriate staining may show basophile degeneration—elacin. The blood-vessels are mostly profoundly altered. On the one hand there is colloid thickening of the walls (of arterioles?), resulting in occlusion and breaking up into blocks. On the other hand may be seen rarefaction of walls (of venules?) with dilatation. Outside the endothelial lining a scanty collagenous network encloses a chain of spaces enclosing lymphocytes. In the neighbourhood there are a few lymphocytes collected, and some strips and fragments of forming colloid. The weakness of the walls of the blood-vessels explains the tendency to hæmorrhage on bruising; the lack of supporting tissue is also a factor, while on the other hand it permits of immediate closure of vessels completely torn across.

"A still further change is seen here and there in the deeper tissues—coalescence of colloid into larger masses. This in excess leads to the rather firm, waxy nodules seen clinically. Such a nodule consists of two portions—(1) a more compact centre, and (2) a looser periphery. In the former there is no trace of blood-vessels, and only the remains of cells. These consist of groups of small granules and of larger spheres. They can be shown fairly well by hæmatoxylin, which they

retain better than the surrounding colloid. In the peripheral parts the colloid is laid down in long strips or layers, perhaps corresponding with the original connective-tissue bundles. The easily moulded new material has been protected from the influence of movement in the conjunctival fold by proximity to the firm central mass; hence the absence of rounded blocks. Between the strips are numerous cells, mostly plasma-cells, but also eosinophile, and a few polynuclear leucocytes, large 'mast-cells,' and some large branched cells containing much pigment. There are also blood-vessels."

Amyloid substance gives the following reactions:

1. *Iodine Reaction* (*Virchow*).—Mahogany brown with iodine.

2. *Iodine and Sulphuric Acid Reaction* (*Langhans*).—The brown produced by iodine is turned darker or passes into violet, blue, or green on further addition of dilute sulphuric acid.

3. *Methyl-violet or Gentian-violet Reaction.*—Purple or pink, the other tissues being blue.

4. *Methyl-green Reaction.*—Violet, the other tissues being green.

5. *Iodine-green Reaction.*—Violet, after prolonged staining (twenty-four hours), the other tissues being green.

6. *Thionin Reaction* (*Kantorowicz*).—Lilac-blue, the other parts being violet.

7. *Polychrome-methylene-blue Reaction.*—Pink, the other parts being blue.

8. *Bismarck-brown and Gentian-violet Reaction* (*Birch-Hirschfeld*).—Bright red, the other tissues being brown.

9. *Picro-borax-carmin Reaction* (*Neumann*) (*see* Vossius).—Yellow against the red or orange of other parts.

In the fully developed condition large sago-grain masses are visible in the unstained section. The iodine reaction is given best in the fresh state, but is also often successful after hardening.

Some of the amyloid masses lie free in the stroma, but most are surrounded by connective-tissue capsules. They vary from microscopic nodules to large masses easily visible with the naked eye. The smaller ones are homogeneous, often with a few nuclei; the larger are generally convoluted, with clefts and fissures. Amyloid globules are seen free in the tissue and also enclosed in cells; they probably do not originate in the cells, but are taken up by them (Leber). Lying between them in the fibrous stroma are the amyloid and hyaline degenerated blood-vessels. The arteries and capillaries show most change. There is endarteritis, with constriction or blocking of the lumen, the intima being thick, rich in nuclei and fibres. The medium is enormously thickened, homogeneous, with some entangled lymphocytes, the outer layers being made up of thick concentric amyloid scales. The capillary walls are thick hyaline or amyloid rings, with small or no lumen. The veins are least altered.

The substance is also found deposited in the lymphatic spaces, which then form beaded cords, the constrictions corresponding with valves in the lymph-vessels. The endothelium is usually retained. Amyloid substance may be found in the small lymphatics of the blood-vessel walls (Hübner).

The degenerative changes affect other unstriped muscle-fibres besides those of the media of the vessel walls; *e. g.* Müller's muscle may be involved (Vossius). The fibrous tissue itself is attacked, the fibres being increased to three or four times their normal breadth, round, rod, or spindle-shaped, normal or degenerated, nuclei being scattered amongst them.

The final stage is the development of bone in the amyloid material. This occurs especially in the neighbourhood of vessels. Osteoblasts are laid down upon the masses, attacking and eroding them. Calcium salts are deposited, and finally scales of true bone, with characteristic bone-corpuscles, are formed. Giant-cells are often found applied to the nodules.

The exact *rationale* of the formation of amyloid masses is a subject of dispute, which belongs rather to general pathology, and cannot be fully entered into here. Some regard the process as taking place essentially in the lymphoid cells, the affection of the connective tissue being secondary (v. Recklinghausen, Leber, Raehlmann); others look upon the cells as being purely passive (Ziegler, Birch-Hirschfeld, Vossius). It is probable that the change occurs in inert proteid exudates and secretions, dominated, however, by the activity of the living cells. That intra-cellular hyaline globules also occur cannot, however, be denied.

v. Recklinghausen.—Handb. d. allg. Path. des Kreislaufs, 1883. v. Oettingen.—Dorpater med. Z., ii, 1871. Reymond.—Ann. di Ott., iv, 1874. Leber.—A. f. O., xix, 1, 1873; xxv, 1, 1879; li, 1, 1900. Raehlmann.—Virchow's Archiv, lxxxvii; A. f. A., x, 1881. *Kubli.—A. f. A., x, 1881. Kamocki.—C. f. A., x, 1886. Vossius.—Ziegler's Beiträge, iv, 1888; v, 1889. Hübner.—B. z. A., xxxviii, 1899. Colucci.—Ann. di Ott., xxix, 1900. Herbert.—T. O. S., xxii, 1902. Dimmer.—Z. f. A., ix, Ergänzungsheft, 1903.

Xerosis

Xerosis of the conjunctiva is a symptom and not a disease. As its name implies, it is characterised by dryness of the conjunctiva. It occurs in two groups of cases: (1) associated with general disease; (2) as a sequel of local ocular affection.

The first type occurs in two forms: (*a*) a mild form, found in adults, accompanied by nyctalopia, and characterised by *Bitot's spots*, small triangular patches on the outer and inner sides, covered by a material resembling dried foam, which is not wetted by the tears; (*b*) a severe form, found in marasmic children, associated with keratomalacia and necrosis of the cornea. Both these forms probably result from malnutrition.

The second type occurs as a cicatricial degeneration of the conjunctiva—(*a*) following trachoma, burns, pemphigus, diphtheria, etc., commencing in isolated spots, ultimately involving the whole conjunctiva and cornea; (*b*) following exposure, due to ectropion or lagophthalmos.

In all cases the principal anatomical changes are found in the epithelium, which becomes thickened and epidermoid, at the same time undergoing fatty degeneration. Leber first described sections

through the whole thickness of the membrane. The superficial cells are flattened, and their nuclei have disappeared; the deeper layers consist of prickle-cells, often widely separated by spaces in which leucocytes are found. The nuclei of these cells stain well, and are surrounded by a clear zone, outside which there are numerous fat globules; these, however, are much more numerous in the flattened cells. Much of the fat is due to the secretion of the Meibomian glands, which is increased. If the fat is removed by soap the cells become capable of being wetted by the tears.

The surface of the epithelium is for the most part even; but here and there the deeper cells are irregularly clumped together and separated from their neighbours, and these balls of epithelium often project above the surface, and later become free in the conjunctival sac (Kuschbert). They contain numerous intra- and extra-cellular "xerosis" bacilli, which grow rapidly under the conditions which exist, but are not the cause of the complaint.

Baas found few leucocytes between the deeper cells. Changes in the protoplasm and nuclei commenced in the middle layers. The protoplasm showed uneven staining—either a clear or a deeply stained zone around the nucleus, or general faint staining; there were also vacuoles. The nuclei stained less than normal, especially at the periphery; in other cells the centre was less stained, so that the nuclei assumed the signet-ring form. The fat globules stained deeply with osmic acid, so that the superficial cells often became filled with reduced osmium.

Attention has more recently been devoted to the horny changes which take place in the more superficial cells (Dötsch, Basso). Those slightly below the surface show granules in the cytoplasm which stain very deeply with hæmatoxylin. The granules consist of keratohyalin, and the layer in every respect resembles the stratum granulosum of the epidermis. The horny cells upon the surface stain very deeply in a diffuse manner, showing no granules. The cells here are often united into long wavy bands or lamellæ (Basso).

This epidermoid condition of the conjunctiva has been called *tyloma conjunctivæ* by Gallenga and Best. It probably occurs in rare cases as a congenital malformation—the simplest type of dermoid (*see* "Epithelial Plaques").

Keratohyalin, besides staining deeply with hæmatoxylin, also stains by Gram's method, differing from other substances in retaining the stain when treated with acid alcohol (Ernst). It also stains with Weigert's fibrin stain, and becomes deep blue with iron hæmatoxylin (Apolant). The strong affinity for hæmatoxylin is shown by Unna's method, in which overstained sections are differentiated with potassium permanganate solution. Keratohyalin shows the red fuchsin stain with van Gieson's method, whereas the more advanced horny material in the superficial cells stains yellow.

BITOT.—Gaz. hebdomadaire, 1863. LEBER.—A. f. O., xxix, 3, 1883. KUSCHBERT.—Deutsche med. Woch., 1884. WEEKS.—A. of O., xv, 1886. BAAS.—A. f. O., xl, 5, 1894. GALLENGA.—Ann. di Neuropath., 1890. SCHIMMELPFENNIG.—A. f. O., xliii, 1897. STEPHENSON.—T. O. S., xviii, 1898. BEST.—B. z. A., xxxiv, 1899; K. M. f. A., xxxviii,

1900. *Dötsch.—A. f. O., xlix, 2, 1900. Basso.—Ann. di Ott., xxix, 1900. Ernst.—Arch. f. mikr. Anat., xlvii; Ziegler's Beiträge, xxi. Apolant.—Arch. f. mikr. Anat., lvii, 1901.

Pinguecula

Pinguecula is a triangular patch on the conjunctiva, found usually in elderly people, especially those exposed to dust, etc. It occurs in the direction of the palpebral aperture, the apex of the triangle being directed outwards. It affects the nasal side first as a rule, the temporal later. The upper border is a little above the horizontal meridian; when large, the inner and outer pingueculæ may meet below the cornea, never above. It has been seen as early as fifteen, and is probably very slow in development. It may encroach upon the cornea, these cases forming early stages in the formation of pterygium. It is greyish in colour, with yellow spots, which may be so numerous as to make it appear yellow throughout. The spots seen with a *loupe* are of irregular shape, the largest and most deeply coloured being often at the edges. Isolated spots are often seen beyond the edges.

The early theories and investigations are of historical interest, but are often inaccurate. The yellow coloration was thought to be due to deposits of fat,—hence the name. Weller first proved this was not so. Saemisch described a thickening of the epithelium, fibrosis of the submucosa, and obliteration of vessels. Robin and Alt laid stress upon the thickened epithelium; Seitz, and Wedl and Bock, upon the fibrosis, Wedl and Bock mentioning the formation of clumps of yellow pigment. v. Michel described proliferation of elastic tissue, the tunica propria being infiltrated by a colloid material. Vassaux found thinning of the epithelium, with patches of cornification, and colloid deposits in the stroma, which did not give an amyloid reaction. Gallenga pointed out the preference for the nasal side, and found thickening of the epithelium, with cornification. The deeper layers of the epithelium and the stroma contained pigment, to which the yellow colour was ascribed. This observation was doubtless due to the fact that the material was obtained rom dark southern races. Proliferation of elastic tissue was noted.

Fuchs made an exhaustive examination of twenty cases derived from the cadaver; the investigation included flat and teased preparations, as well as serial sections. The essential changes are found in the substantia propria, and consist in deposits of amorphous hyaline material, hyaline degeneration of the fibrous tissue, and proliferation of elastic tissue.

The amorphous hyaline material is deposited in the form of fine granules, especially in the superficial layers. They lie free in the interfibrillar spaces, and fuse into irregular angular grains. The grains fuse into irregular nodules, with a smoother contour. They are arranged in places along the walls of the vessels, which may have also undergone hyaline degeneration; in this manner a radial disposition is shown, often marked in those cases which extend below the cornea. The deposits are insoluble in strong mineral acids, alkalies, ether, chloroform, etc. They stain deeply with alum carmin, eosin, acid fuchsin;

only the larger ones are stained by hæmatoxylin. They give no amyloid reaction. They are therefore allied to v. Recklinghausen's "hyalin." The nodules often fuse into larger concretions, which may be visible with the naked eye (over 0·1 mm.). The largest of these only stain at the edges with hæmatoxylin. They seem to approach the condition of amyloid, staining brown with Lugol's solution (iodine), but they never stain pink with methyl violet.

The loose subconjunctival fibrous tissue also shows hyaline degeneration. The fibres become thicker and more homogeneous; they also grow in length and become convoluted. The nuclei are often hidden, but not degenerated. The degeneration is not uniform, but patchy. Several clumps are often connected by a strand, which may represent a degenerated vessel. They are often covered by an endothelial membrane, which represents the normal structure. Deposits of granules take place in parts of the larger clumps, and these may go on to form concretions. The same process occurs in less degree in the superficial scleral lamellæ, only those concentric with the cornea being usually affected, the meridional ones escaping. This is probably an intercurrent phenomenon, having nothing to do with pinguecula proper.

Normally, only the subconjunctival (episcleral) tissue is rich in elastic fibres. In pinguecula these are increased in number, in calibre, and in length, so that they become convoluted and form knotty heap They proliferate into the submucosa, and the whole thickness of the substantia propria may be pervaded by close parallel bands of elastic fibres. The convoluted clumps are often large enough to be seen with the naked eye, and compose one form of the yellow spots. The more swollen fibres (over 0·03 mm.) are often loosely arranged, and break up into fragments of various sizes and lengths. Some show a deeply stained (hæmatoxylin) central band, with a lighter irregular sheath; others are longitudinally fibrillated. Hypertrophy of the elastic fibres not only pervades the conjunctiva and the episclera, but also the surface layers of the sclera. Here they appear as spiral or convoluted bands between the lamellæ. The swollen fibres often go on to the formation of hyaline concretions as well as the white fibres, but these are not so frequent or so large, and are less regularly contoured.

In typical sections through a pinguecula the following layers can be made out, though often not in a single section:—(1) Epithelium, (2) submucosa, (3) pinguecula proper, (4) layer of hyaline fibrous tissue, (5) layer of loose subconjunctival tissue, (6) episclera, (7) sclera.

1. *The Epithelium.*—This is modified conjunctival epithelium. In the depressions it may be quite normal, with basal cubical cells having deeply stained nuclei, round or polygonal cells in several layers, and superficial cylindrical cells. On the eminences, where it is exposed to the pressure of the lids, the epithelium becomes flattened, and may even be reduced to a double layer of flat nucleated spindle-shaped cells. The smaller depressions are filled in with epithelium, the surface remaining smooth (levelling tendency of epithelium [Fuchs]). Cornification is excessively rare. Pigment may be present as in normal conjunctiva, but is not increased. "Colloid degeneration" (de Vincentiis),

i. e. vacuolation of the cells and their nuclei, may occur as in pterygium (q. v.), and may affect all the cells except the basal ones. Concretions may invade the epithelium, which is thinned over them and may be destroyed. They are not formed *in situ.* Psorosperms may be present (Fuchs).

2. *Submucosa.*—This is normal at a short distance from the limbus, consisting of wavy fibrous tissue with many cells and vessels. Near the cornea it is thin and very dense, showing only a delicate striation, with very few cells and no blood-vessels. It is raised *en masse* into waves by the underlying nodules. The submucosa and the next layer tend to invaginate the cornea, so that the epithelium or the superficial corneal laminæ, or both, are invaded. This forms the earliest development of the pterygium.

3. *The Pinguecula Proper.*—This consists of a thick mass with irregular surface, containing scarcely any nuclei or vessels. Under a low power it looks homogeneous; under a higher power it is seen to consist of dense bands of fibrous tissue, mostly running meridionally, but with areas of circular fibres cut across. Amongst these are embedded masses of hyaline deposits, hyaline and elastic fibres, and concretions.

4. *Layer of Hyaline Fibrous Tissue.*—This runs chiefly meridionally, with nodules of hyaline fibres cut across here and there.

5. *Layer of Loose Subconjunctival Tissue.*—This shows in places the changes from which the nodules are later developed, viz. fine granules and small nodules, with thickened elastic fibres.

6. *Episclera,* with small knots of enlarged elastic fibres.

7. *Sclera,* with hypertrophied elastic fibres, and occasionally hyaline lamellæ.

The changes, therefore, are essentially degenerative, and are attributable to prolonged irritation by dust, smoke, etc., and age. More recent observations by Sgrosso, Hübner, and others, confirm the facts brought forward by Fuchs. Sgrosso distinguishes an episcleral and a conjunctival pinguecula, the latter being further subdivided into epithelial and fibrous, the last named being the commonest. Hübner lays more stress upon the elastic fibres, which were demonstrated by the Tänzer-Unna orcein method, than upon the hyaline degeneration. The elastic tissue showed degeneration allied to that found by Unna and others in the skin. There can be little doubt that the increase in elastic tissue is the main cause of the yellow colour in pinguecula, and is the essentia element.

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PTERYGIUM

Pterygium is a peculiar encroachment of the conjunctiva upon the cornea. It is triangular in shape, and when single is always upon

the nasal side. When double, the temporal one has developed later. It is derived from pinguecula, and therefore only occurs in the situations mentioned. It must be carefully distinguished from the pseudo-pterygium, a fold of conjunctiva adherent to the cornea, which has been previously ulcerated. The latter may occur at any part of the cornea; the conjunctiva forms a bridge over the limbus, and a fine sound can always be passed beneath it. This is not possible with a true pterygium.

The apex of the pterygium is usually blunt, the classical description of a sharp apex applying only to rare cases. This anterior border generally slopes from up and in to down and out, and is irregular. There is no ulcer in the cornea beyond it, as formerly described, but there are often small opacities, which gradually fuse with the edge and partly cause its irregularity. The anterior border has a grey, gelatinous margin, and is often as much as 1 mm. thick; the numerous vessels of the pterygium do not enter this part. Sometimes it is nearly flat and star-like; these are probably stationary pterygia. There are two main folds at the upper and lower borders of the pterygium, diverging as they pass away from the cornea. These are due to the traction upon the conjunctiva, and in advanced cases are multiplied by subsidiary folds. There is no passage beneath the neck at the limbus, but only pockets above and below, so that the pterygium is a single layer of conjunctiva, and is adherent in its whole length to the sclerotic and cornea, though only loosely, except at the apex. The area of adhesion to the cornea is always smaller than the breadth of the head, but is very irregular. The traction on the conjunctiva often pulls the plica semilunaris out of place, so that its upper end is pulled outwards, and it may even lie horizontally. It is recognisable as a deep red line. There are often yellow spots in the pterygium, but always fewer than in a pinguecula. Cysts may be visible rarely, usually in the head, never in the grey zone.

The earlier histological investigations are merely of historical interest, as they are frequently inaccurate, having been made upon excised fragments. Getz found inflammatory changes. Winther regarded the pterygium as an overgrowth of corneal tissue. Schreiber thought it was covered on the deep surface with epithelium and was due to an adherent polypous growth of the conjunctiva. Arlt, Goldzieher, Poncet, Harder, and Gallenga examined pterygia still attached to the globe. Their results are contradictory. Mannhardt regarded episcleritis as the starting-point, but he also described the gradual encroachment of pinguecula upon the cornea. Zehender first derived pterygium from pinguecula, but gave no proofs. Arlt considered it to be a mere fold of conjunctiva, adherent to a marginal ulcer. If this were so it should be common in children after phlyctenular conjunctivitis. An ulcer was described as present beyond the tip of the fold, and as it advanced across the cornea the fold of conjunctiva was dragged after it.

The histology of pterygium has been worked out very fully by Fuchs, and the following is a *résumé* of his paper:

The pterygium is covered by conjunctival epithelium for the greater

part of its surface (Fig. 54). It differs much in thickness, being thin on the exposed parts and thick where small irregularities in the stroma are filled in. It is stratified, with flat cells upon the surface, but these become cylindrical in the folds and furrows, and also where the normal conjunctiva is approached, *i.e.* away from the apex. Where pigmentation is normally present, as in dark people, it is increased, especially in the basal cells, but it may occur in all the layers as well as in the stroma. In the middle layers there are often intercalated stellate cells, whose nuclei and protoplasm stain more deeply than the others. They have single round nuclei and ample cytoplasm, so they are not leucocytes (Fuchs). Rarely there are hyaline nodules in the epithelium, and also psorosperm-like cells. The latter are commonest in the furrows. Some of the cells show vacuolation of the nuclei

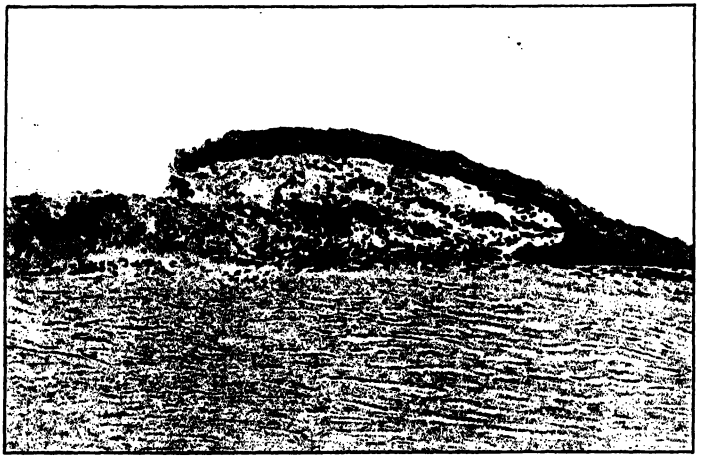


FIG. 54.—PTERYGIUM. × 100.

Small pterygium on inner side of cornea, from a man aged 75. Note hyaline degeneration and granular deposits in fibrous tissue to the left. The new tissue is as yet entirely superficial to Bowman's membrane, which can be faintly traced in the figure.

("colloid degeneration"), the chromatin being pressed down into a crescent at the lower border. Goblet-cells are numerous, especially in the depressions. True new-formed glands are usually, though not invariably, present. They occur only in the body of the pterygium, some millimetres from the limbus. They are tubular depressions, lined with cylindrical cells, upon a basis of flattened epithelial cells. The inner layer is often full of goblet-cells. The tubules often run horizontally under the epithelium and branch; they may be surrounded by lymphocytic infiltration, but this is often conspicuously absent in all parts. Sebaceous glands and hair-follicles may be found in the base, but these belong to the caruncle, which has been pulled outwards. Cysts may be formed out of any of the glands or depressions, and often contain secretion and *débris*. The transition from conjunctival to

corneal epithelium is much sharper than normal at the apex of the pterygium. In most cases it is covered by corneal epithelium, in some the conjunctival extends a short distance over the cornea, and this is the rule for the sides. Occasionally the limit between the epithelia is vertical, but often the conjunctival thins off over the corneal, and is quite distinguishable from it by the cells being smaller and more deeply stained. The corneal epithelium is often thickened at the margin.

The stroma is loose and rich in cells. It differs only from normal conjunctiva in that the fibres are drawn out by the traction, and run parallel instead of in waves. At the anterior border it may be either loose, cellular, and rich in vessels, or dense and firmly fused with the cornea. The denser apex moves forwards as the pterygium grows, leaving looser tissue behind it. Patches of hyaline degeneration of the fibres and vessel walls occur as in pinguecula, but are much less evident. Masses of enlarged elastic fibres may also be present.

Bowman's membrane is either completely destroyed under the pterygium, or is only present in fragments. It is always destroyed for some distance beyond the apex in young pterygia (as much as 3 mm. [Fuchs]); in the oldest it stops exactly at the apex, or extends a short distance under or into the apex. Farther from the apex, where Bowman's membrane is still intact, there are changes which are seen with the *loupe* as islands of opacity. Here Bowman's membrane may be destroyed over a small area, and be replaced by loose lamellæ with a few nuclei. The basal epithelial cells generally lie obliquely here, bending over towards the defective spot. Or a small mass of dense fibrous tissue, with long nuclei, may lie above or below Bowman's membrane, forming a depression in it without completely destroying it. Where Bowman's membrane stops it may be cut off straight or obliquely, or be pointed, or break up into fibres. It is not infrequently bent round or folded. There are always fragments of Bowman's membrane found under a large pterygium.

When the anterior border of the pterygium consists of loose tissue it always penetrates amongst the superficial corneal lamellæ. Some of these are raised up, so that they curve forwards or may even turn back in the opposite direction. They are finer than normal, and have clefts between them. They are also more cellular, and may be infiltrated with round-cells. They may be much folded and bent, and if Bowman's membrane is present it follows the curve, or the lamellæ may bend over the end of it, so that they come to lie in front. This may also occur at the sides and beneath the pterygium. When the anterior border consists of dense fibrous tissue it pushes its way between the epithelium and Bowman's membrane, here and there encroaching upon the latter. The corneal lamellæ are here little altered. This type probably represents the stationary pterygium, whilst the other is progressive. Both types occur in the same anterior border, but growth is often unequal in different parts.

These anatomical characteristics quite disprove Arlt's view that pterygium is caused by adhesion of conjunctiva to a progressive ulcer, and is gradually drawn forwards as the ulcer cicatrises behind. It

seems probable that it is due to altered nutrition in the cornea, due to the presence of a pinguecula, combined probably with some chemical changes which manifest themselves in advance of the apex of the actual pterygium, and lead to tissue changes (histiolysis) there. The pinguecula doubtless impedes the flow of blood in the vessels of the limbus, and may lead to local atrophy of the marginal network.

Recurrent pterygium shows the same structure as primary (Bocchi).

Hübner's researches on forty pterygia confirm those of Fuchs; but more stress is laid upon the presence and degenerative changes of the elastic tissue, as seen by the orceïn method. Sections stained by acid orceïn and van Gieson show the distribution of the white and yellow fibrous tissue well. Hübner considers pterygium independent of pinguecula, though both may occur together.

ARLT.—Die Krankheiten des Auges, i, 1854. ZEHENDER.—Handb. der ges. Augenheilk., 1869. SCHREIBER.—Inaug. Diss., Leipzig, 1872. POWER.—St. Bart.'s Hosp. Rep., 1875. GOLDZIEHER.—C. f. A., ii, 1878. PONCET.—A. d'O., i, 1881. HARDER.—Mittheil. aus der k. Univ.-Augenkl. zu München, i, 1882. MANNHARDT.—A. f. O., xxii, 1, 1876. GALLENGA.—Giorn. d. R. Accad. di Med., Torino, 1888. *FUCHS.—A. f. O., xxxviii, 2, 1892. BOCCHI.—Arch. di Ott., ii, 1894. *HÜBNER.—A. f. A., xxxvi, 1897. TRAPESONTZIAN.—A. d'O., xxi, 1902.

PIGMENTATION

Spots and patches of pigment occur normally at the limbus in dark-coloured races, and in them, too, the epithelium contains pigment granules, especially in the deeper layers, and there are more chromatophores in the subconjunctival tissue than in the fair races. In dark races the pigment also occurs in branching cells amongst the epithelial and subepithelial cells.

Pigmented spots in the conjunctiva in the white races are always suggestive of malignant disease (*v. infra*). Diffuse pigmentation occurs very rarely, and is apt to spread. It may terminate in death from melanotic sarcoma in other organs, but whether the conjunctival melanosis is primary or secondary is undecided. In one case which I examined the patient was apparently healthy, apart from increasing pigmentation of the conjunctiva and cornea. On microscopic examination the pigment formed clumps almost entirely confined to the epithelium; there were a few masses just below the epithelium in the conjunctiva. The pigment contained no iron, and was readily bleached.

ARGYROSIS

Argyrosis of the conjunctiva has been examined microscopically by Junge, Knies, Hoppe, and others; Frommann, Riemer, and Neumann investigated particularly pigmentation following prolonged internal administration of silver nitrate. The anatomical results are similar, whether due to internal or external use.

Hoppe found the pigmentation greatest in the lower and middle

third of the conjunctival sac; the intermarginal zone at the edge of the lid was normal; the lower punctum was more deeply stained than the upper.

Microscopically the coloration is chiefly due to staining of the elastic fibres, which are beautifully demonstrated; less to pigment free in the tissues. The pigment is everywhere in the form of extremely fine black granules. The granules separate out on treatment with concentrated hydrochloric acid, and become yellow and highly refractile; on addition of ammonium sulphide they become black from the formation of silver sulphide. The granules are decolourised by concentrated nitric acid; they remain unaltered with caustic potash, though the fibres swell up. The pigment is dissolved by potassium cyanide, and decolourised, with the formation of silver iodide, by iodine solution.

The granules therefore consist of an almost insoluble ground substance, with a superficial black deposit. Hoppe found none intra-cellular, so that leucocytes apparently play no part in carrying the pigment. It seems to ensheath the elastic fibres, without entering into any chemical combination; some fibres remain unaltered, as shown by Weigert's elastic stain.

There is a thin, nearly continuous layer of free pigment immediately under the epithelium of the palpebral conjunctiva; this is absent in the bulbar conjunctiva, where the free pigment pervades the tissues uniformly like an emulsion.

The adventitia of the vessels is free from staining, whilst the pigment is dusted over the media, lying thickly in the cement substance between the muscle-fibres; in this manner transverse stripes are marked out. In the capillaries the pigment is deposited in the cement substance between the endothelial cells.

The epithelium is free from pigment. The elastic fibres are seen to be arranged in a superficial layer of large bundles, running mostly vertical to the surface, and a deep layer of fine fibres, forming a dense network.

JUNGE.—A. f. O., v, 2, 1859. FROMMANN.—Virchow's Archiv, xvii, 1859. RIEMER.—Arch. f. Heilkunde, xvi, 1875. NEUMANN.—Stricker's Med. Jahrb., 1877. KNIES.—K. M. f. A., xviii, 1880. *HOPPE.—A. f. O., xlviii, 3, 1899.

CYSTS

Small cysts of the conjunctiva are not very rare, and probably often escape detection. Out of sixty-five published cases, five were in the C. palpebrarum, nineteen in the fornix, thirty-two in the C. bulbi, and nine elsewhere (Ballaban). They arise from a great variety of causes, and the exact pathology of many of them is disputed. Cirincione has recently published a monograph upon the subject, in which the following classification is adopted:—I, Congenital cysts; II, Acquired cysts; III, Lymphatic cysts; IV, Parasitic cysts; V, Traumatic cysts. Groups III, IV, and V really belong to Group II, but are separated

on account of their importance. The acquired cysts are further divided into superficial and deep. The superficial cysts are subdivided as follows:—(1) Cysts with transparent contents (serous cysts), including (*a*) cysts of the fornix, (*b*) cysts of the C. bulbi; (2) cysts with opaque contents; (3) cysts containing bacteria; (4) false cysts. The deep cysts include (1) cysts of Krause's glands; (2) parasitic cysts (cysticercus, filaria).

This classification seems unnecessarily complicated. I shall consider cysts of the conjunctiva under the headings (1) Traumatic, (2) Retention, (3) Lymphatic, (4) Pseudo-cysts, (5) Parasitic, (6) Congenital. The term "serous cyst" is better avoided; it usually includes lymphatic and some retention cysts.

BALLABAN.—A. f. A., xliii, 1901. *CIRINCIONE.—B. z. A., lv, 1903. POSSEK.—Z. f. A., ix, Ergänzungsheft, 1903 (Bibliography).

TRAUMATIC CYSTS

Cysts occasionally develop in the conjunctiva after injury, especially at the site of tenotomy wounds, or around foreign bodies. These are implantation cysts, due to the inclusion of epithelium, which subsequently grows, degenerates in the centre, and forms a cyst. Only three such cases have been submitted to careful histological examination (Uhthoff, Treacher Collins). In one the cyst appeared five weeks after a strabismus operation, in a woman of twenty; in another five weeks after a wound which perforated the upper lid and injured the globe. In each the cyst was lined by stratified epithelium. In one there were several cilia, partly fixed, partly loose, some projecting outside. The epithelium had proliferated around them inside the cyst. Treacher Collins's case was a boy aged nine, whose eye was wounded by a screw-driver at the age of nine months. There was a scar vertically across the inner part of the cornea, and a cyst just beyond the limbus below. The latter was found to lie between the conjunctiva and the sclerotic, not communicating with the anterior chamber. It was lined with laminated epithelium.

These cysts are generally fixed to the sclerotic by inflammatory tissue, and cannot be moved so freely as the lymphatic cysts. Like them, however, they contain a simple serous fluid.

Cirincione doubts the existence of traumatic cysts. In one case which he examined he found a cysticercus.

UHTHOFF.—Berl. klin. Woch., 1879. TREACHER COLLINS.—Researches, London, 1896. LOPEZ.—A. f. O., xxi, 1892. LANGE.—K. M. f. A., xli, 1903.

RETENTION CYSTS

Retention cysts in the conjunctiva are usually small, developed in new-formed glands, the result of inflammatory processes, and in the so-called Henle's glands; they also occur rarely in Krause's glands.

As has been mentioned, Henle's glands are really folds in the conjunctiva, but true tubular glands are occasionally present, and are

certainly developed by inflammatory processes. Moreover every mucous membrane, apart from goblet-cells, is a secreting surface, and when it is swollen and inflamed the depressions are liable to be shut off from the surface by the apposition of the folds. The secretion is increased by the inflammation, and the goblet-cells are multiplied. The mucus and serous fluid are retained, and give rise to cysts. Originally tubular, with many diverticula, especially in the fornix, the glands become dilated and globular, or polyhedral from mutual pressure. The walls, like the surface, are formed of a double layer of epithelium, the inner layer being cylindrical with the nuclei towards the bases of the cells. But this regularity is not maintained. The pathological processes lead to proliferation and degeneration of the cells. In parts the epithelium is heaped up; in others the pressure of the retained secretion is more felt, and flattening of the cells occurs. The goblet-cells are often much increased in numbers, so that the lumina are lined with them. Other cells become œdematous, often become loosened from their attachments and lie free in the cavity, there to undergo further degenerative changes. The retained fluids and *débris* alter chemically, and often form concretions (q. v.).

These cysts have been studied by Rogman, Ginsberg, Fuchs, Wintersteiner, Stoewer, and others. In Rogman's case the epithelium varied from two to eight layers, and formed many papillary ingrowths into the lumen. Ballaban describes cysts in the conjunctiva which he attributes to degeneration of the central cells in solid downgrowths of epithelium (Fig. 34). The process was evident in the younger columns, the cells showing vacuolation; later, hyaline concretions were formed. The fully developed cysts were lined with a varying number of rows of cells, the larger the cyst the greater being the degeneration and the thinner the epithelial lining.

Less aberrant are the cysts of Krause's glands. These have been especially studied by de Vincentiis and his pupils. Wintersteiner regards the cases of Gallenga, de Vincentiis, Moauro, Antonelli, and Stoewer as genuine; those of Rombolotti, Bull, Camuset, and Rampoldi and Faravelli as doubtful. They are generally small, and lie in the upper or lower fornix; hence they cannot be due to Waldeyer's glands. The cysts are evidently formed in a tubular gland with many convolutions, so that they cannot be due to Henle's glands; moreover they lie deeper. The lining epithelium varies, being cylindrical in the more normal parts, flattened and pathologically altered in other parts. It may form a single or a double layer, but the surface epithelium often proliferates and forms several layers, the inner cells being loose and free in the lumen.

The cysts often form in part of the duct, which normally has a double layer of epithelium, the inner layer being cubical. Sometimes only part of the duct is cystic; there is then a triangular depression, forming the mouth, at the conjunctival surface. The acini in connection with the cystic duct generally atrophy. Each cyst is unilocular, but several may be present, and a single one may give the appearance of many when the walls are collapsed and folded. Concretions with giant-cells occurred in Wintersteiner's case. As there was no break in

the epithelium and no granulation tissue, the giant-cells must have been formed either from leucocytes or from epithelial cells, either by nuclear division or by confluence of cells. Antonelli also found concretions, in his case derived from blood-corpuscles.

The relative infrequency of cysts of Krause's glands is to be attributed to the fluidity of their secretion (Ischreyt), and to their slight powers of resistance (Wolfring). Blocking of the ducts is apparently due to cicatricial contraction from injury (Rombolotti), trachoma (Moauro, Wintersteiner), and inflammatory infiltration (Ischreyt). In many cases the conjunctiva was otherwise normal.

Another case reported by Wintersteiner, and others by Vossius, Rampoldi and Faravelli, etc., would seem to be developed in congenital atypical glands.

The cysts which occur in old trachomatous granulations are really retention cysts in new-formed glands (*v.* p. 69).

Cirincione found the superficial cysts of the fornix to be either uni- or multi-locular; they might be as large as a small bean. The wall consisted of a structureless membrane lined by a double layer of epithelium. The inner layer varied greatly, consisting in some cases of cubical cells with round nuclei and little protoplasm, in others of cells in which the cell body seemed to be replaced by a hyaline drop, the nucleus being pressed towards the base. The outer layers of cells were flattened, with round, more deeply staining nuclei. The cubical cells were absent in the large cysts, and often in places elsewhere. The contents of the cysts varied greatly, being generally hyaline, often granular. The substance consists of the mucus secreted by the goblet-cells, mixed with cell detritus. Some cysts contained small brown granules, which were probably reduced silver, the result of treatment with silver nitrate. Others contained curious ovoid bodies, with double contour, from 15 μ to 50 μ in diameter, containing a nucleus-like body. They were probably degenerated cells; the possibility of their being parasites was considered.

Cirincione denies the new formation of true glandular depressions in the conjunctiva in inflammatory conditions, supporting his contention on the absence of such an occurrence elsewhere in the body. On the other hand, by means of an exhaustive research by serial sections, he found a few true crypt-like glands in the conjunctiva of a seven and a half months' fœtus, the ordinary folds and furrows being absent at this age.

Cirincione found serous cysts of the bulbar conjunctiva much rarer than those of the fornix, if lymphatic cysts are eliminated. They were never more than 3 mm. in diameter, and lay rather deep, about half-way between the surface and the sclerotic. There was usually only a single layer of flattened epithelium. In spite of Cirincione's opinion, it would seem likely that these were really lymphatic cysts.

Cirincione found superficial opaque cysts of the conjunctiva in subacute trachoma. They were small, ovoid, ash-grey, generally situated at the convex border of the tarsus. They are apparently due to degeneration of the acini of Krause's glands. The stroma is at first densely infiltrated with round-cells; the duct loses its epithelium

in patches. Later, the gland-cells swell and show hyaline degeneration, running together and losing their definite contours, until the parenchyma becomes transformed into a transparent mass, containing nuclei and a few recognisable acini. Finally a cystic space is formed, lined with a double layer of epithelium, inner cylindrical and outer cubical, resembling the lining of the ducts. It contains a granular mass consisting of degenerated cells and *débris*.

Cirincione only found bacteria in small round cysts, about the size of a pin's head, near the posterior border of the tarsus. They were greenish and opaque. They contained very small micrococci, rarely bacilli. The organisms stained best by Gram's method. The cysts were formed from conjunctival crypts; they contained many cells, and were surrounded by inflammatory infiltration. They were lined with enormous goblet-cells lying on a layer of flattened cells.

Cirincione calls "false cysts" those which are formed in chronic inflammatory conditions amongst the folds and papillary outgrowths of the conjunctiva. The false papillæ are often pressed together so that secretion is retained in the depressions between them. These are not true cysts, since the depressions are not true glands. They are never larger than a pin's head, contain secretion, cellular *débris* and leucocytes, and are rarely lined with cubical epithelium. Cirincione considers that the cysts in old trachomatous lids originate from such false cysts. It is probable that many are retention cysts of the Meibomian and other glands, following cicatrisation around the ducts.

Cirincione's "deep cysts" are retention cysts of Krause's glands. They are found chiefly at the lateral parts of the fornices, are smooth-walled and oval, with the long axis transverse. They are most common in young people, with trachoma or chronic catarrh.

The cysts are lined with a double layer of epithelium, inner cubical or cylindrical, outer flattened. In the more distended parts or cysts there is only a single layer of flattened cells. The neighbouring acini vary, some being normal, others compressed by the cystic condition of the duct, or themselves dilated into cysts.

ROGMAN.—A. d'O., xv, 1895. GINSBERG.—A. f. O., xliv, 1, 1897. FUCHS.—A. f. O., xlvi, 1, 1898. WINTERSTEINER.—A. f. O., xlvi, 2, 1898. STOEWER.—A. f. O., liv, 1902. BALLABAN.—A. f. A., xliii, 1901. RAMPOLDI AND FARAVELLI.—Ann. di Ott., xvii, 1888. MOAURO.—Ann. di Ott., xviii, p. 251, 1889. ANTONELLI.—Ann. di Ott., xix, 1890. ROMBOLOTTI.—A. f. A., xxxi, 1895. MAKROCKI.—K. M. f. A., xxi, 1883. STOEWER.—K. M. f. A., xxx, 1892. ISCHREYT.—A. f. A., xxxv, 1897. BULL.—Amer. Jl. of Med. Sc., 1878. VOSSIUS.—B. d. o. G., 1896. WOLFRING.—VII internat. Kongr., Heidelberg, 1888. ACKERMANN.—A. f. A., xlvi, 1902. * CIRINCIONE.—B. z. A., lv, 1903.

LYMPHATIC CYSTS

Lymphatic cysts cannot be pathologically differentiated from lymphangiectasis and lymphangioma (q. v.), but are locally exaggerated manifestations of the same condition. They are confined to the C. bulbi. In the intermediate stages certain of the dilated lymph-spaces become much enlarged, and the fluid cannot be pressed from these into the smaller ones. Later, these develop into true cysts, which may be sessile or pedunculated, are yellowish and transparent,

and vary in size, but are never very large. They grow partly by the fusion of smaller dilatations. They differ from the epithelial serous cysts in not being definitely oval or round, and in never being single. Even when they are apparently single clinically, they are found to be multilocular on examination. The large cyst reported by Snell and described by Treacher Collins would appear to be an exception to this rule, but the fact that it was present from birth makes its true nature doubtful. It was lined throughout by a single layer of endothelial cells.

Histologically these cysts have the same structure as the lymphangiomatous spaces.

Priestley Smith.—Brit. Med. Jl., 1883. Snell.—T. O. S., xviii, 1898. Sgrosso.—Ann. di Ott., xxxi, 1902.

Pseudo-cysts

In addition to the "false cysts" described by Cirincione (*v.* p. 115), there are others, of which the following are examples:

Goy describes a large congenital serous cyst in a woman of fifty-nine, occurring in conjunction with other congenital malformations of the eye. It was not a lymphatic cyst, but probably a pseudo-cyst developed from symblepharon. It was lined with stratified epithelium, and encroached upon the cornea.

Subconjunctival hæmatomata have been accredited with the formation of serous cysts. Mitvalski describes a case of this kind, in which subconjunctival hæmorrhage occurred after vomiting. In fourteen days there developed an oval, elastic cyst, the size of a bean, containing clear fluid, the walls only being infiltrated with blood. These consisted of fibrous tissue, and there was no endothelial or epithelial lining.

Goy.—B. z. A., xxxix, 1899. Mitvalski.—C. f. A., xvii, 1893.

Parasitic Cysts

Parasitic cysts of the conjunctiva are rare, and are due to varieties of cysticercus, C. cellulosæ (that of tænia solium) being commonest. Others are caused by filariæ. The hydatid cyst, due to tænia echinococcus, occurs in the orbit, and may appear as a subconjunctival cyst.

Cysticercus.—The first observation was reported by Baum, in 1838, and since then fifty-five cases have been recorded (Lagrange), or one sixth of all cases of intra-ocular cysticercus (Ballaban). Mackenzie reported two, one borrowed from Estlin and seen at the Bristol Eye Infirmary; others have been published by Canton, Vernon, Werner, Secker Walker, etc., in England. It is commoner in Germany and Russia. It is much less common in the conjunctiva than in the vitreous (v. Graefe, Poncet). It generally occurs in young patients.

Conjunctival cysticercus appears as a hemispherical or oval cyst, usually at the internal angle in the lower fornix; but there are many

exceptions to this situation. Sgrosso found it at the outer angle, Meyer below the cornea, Rohmer in the upper fornix. It is adherent to the sclerotic by an inflammatory capsule, which surrounds it, and is formed of two layers (Makrocki). The inner, adherent to the cysticercus, is made up of embryonic cells; the outer of fusiform cells, with foreign-body giant-cells (Gallemaert, Fuchs). Histological examinations have been made by Binet and Fieuzal, Jani, Mitvalsky, Cirincione, etc.; and Sgrosso inoculated the parasite into the rabbit's orbit and obtained similar results. Bull gives good photographs of the hooklets and cyst wall.

The cyst is pink, almost transparent in the centre, in which there is usually seen a whitish or yellow disc, which is the site of the scolex. There may be some conjunctival reaction, but this is often slight.

The cyst contains, besides the parasite, fluid excreted by it. The fluid contains proteids and leucomains (Mourson and Schlagdenhaufen), and produces acute peritonitis when injected into the abdominal cavity of rabbits.

Filaria.—Filaria loa occurs in residents in the West Coast of Africa, and not infrequently finds its way under the conjunctiva (Wilson, Argyll-Robertson, Gerwais and v. Beneden, Hirschberg, Ludwig). It apparently does not lead to the formation of cysts. An allied species, Filaria inermis (Grassi), was found in a cyst by Cirincione. The cyst walls resembed very nearly those of the cysticercus cyst.

BAUM.—Ann. d'Oc., ii, 1839. MACKENZIE.—Diseases of the Eye, 1839. ESTLIN.—Med. Times and Gaz., 1838. CANTON.—Lancet, 1848. VERNON.—R. L. O. H. Rep., vi, 4, 1869. * WERNER.—T. O. S., ix, 1889. SECKER WALKER.—T. O. S., xvi, 1896. v. GRAEFE.—A. f. O., iii, 2, 1857. PONCET.—Gaz. méd. de Paris, 1874. SGROSSO.—Rev. gén. d'O., xii, 1893. MAKROCKI.—K. M. f. A., xxi, 1883. GALLEMAERT.—Bull. Acad. roy. de Méd. de Belgique, Bruxelles, 1897. FIEUZAL.—Bull. de la Clinique des Quinze-vingts, 1886. JANI.—K. M. f. A., xxi, 1883. FUCHS.—K. M. f. A., xv, 1877. MITVALSKY.—C. f. A., xvii, 1893. BULL.—T. Am. O. S., 1899. * KRAEMER.—Die tierischen Schmarotzer des Auges, in G.-S., x, 1899. CIRINCIONE.—B. z. A., lv, 1903. WILSON.—T. Am. O. S., 1890. ARGYLL-ROBERTSON.—T. O. S., xv, 1895; xvii, 1897. GERWAIS AND v. BENEDEN.—Traité de Zool. méd., ii. HIRSCHBERG.—C. f. A., xx, 1896. LUDWIG.—Z. f. wiss. Zool., lx, 1895.

CONGENITAL CYSTS

Small cysts occur in some congenital tumours, especially nævi (q. v.).

More important are the peculiar cysts of the lower fornix associated with maldevelopment of the eyeball (microphthalmia, etc.). These will be described in connection with congenital malformations.

TUMOURS

POLYPUS

There is a tendency for all tumours of the conjunctiva to assume the polypoid form, and hence several quite different pathological conditions have been called polypi. They are doubtless moulded to this shape chiefly by the movements of the lids and eyes (Axenfeld), and

the direction of least resistance to growth is outwards. True polypus, *i. e.* hyperplasia of a circumscribed portion of the conjunctiva in all its layers, is said to be unknown (Elschnig). So-called polypi are either true papillomata, soft or hard fibromata, or granulation-tissue tumours (granulomata); though other growths, *e. g.* sarcomata, often become polypoid; even dermoids may be polypoid (*v. infra*).

* Elschnig.—A. f. A., xix, 1889. Zimmermann.—K. M. f. A., xxxii, 1894.

Papilloma

Papilloma of the conjunctiva is found most commonly at the inner canthus in the neighbourhood of the caruncle and plica semilunaris. It is also found in the fornices, and Colucci has described a case in which it invaded the whole length of all four fornices. The small,



Fig. 55.—Papilloma of the Conjunctiva. × 9.

The leaflets are composed almost entirely of epithelium, with a fine core of fibrous tissue. The growth came from near the caruncle, and in the centre of the lower part some acini of a sebaceous gland are seen. *See also* Fig. 81.

raspberry-like tumours are also often multiple. They are very prone to recur after removal. They occur at all ages. In some cases they are small, multiple, and very vascular, the vessels being arranged in a star-shaped manner (Burnett). I have seen a good example of this type; the small growths have some resemblance to limpet shells.

Histologically papillomata consist of a central core of fibrous tissue with blood-vessels, covered by stratified epithelium (Fig. 55). Gradations are met with between papillomata with very little fibrous tissue and fibromata with papillæ upon the surface, and various parts of the same tumour may show these peculiarities. The epithelium is generally

greatly increased in thickness, so that it makes up the main mass of the tumour, the supporting connective tissue being reduced to a minimum. Many of the cells, especially upon the surface, are often goblet-cells; the whole surface was covered with them in a case reported by Wagenmann. The blood-vessels are usually very thin-walled, often merely endothelial tubes; they are usually widely dilated. The fibrous tissue may be actually reduced to a few strands around the vessels. The papillæ often divide and subdivide, forming a very complicated mass of leaflets.

As elsewhere in the body, papillomata grow outwards and do not usually invade the deeper tissues, but there can be no doubt that they sometimes become malignant. Examples have been published by Lagrange and Mazet, Kopetzky v. Rechtperg, and Altland, in which papillomata later invaded the globe and became intra-ocular. These cases are rare; epitheliomata with papillomatous proliferation are commoner; both are generally in elderly people. Papillomata, as well as epithelioma (*v. infra*), occur in xeroderma pigmentosum (Sims).

Even when very efflorescent, these growths usually only cover the cornea; in the rare cases in which it is involved, the growth begins between the epithelium and Bowman's membrane (Caspar). In Lambert's case, in which the tumour grew from the limbus, it was partially attached to the cornea. In Altland's cases there had been episcleritis; the author discusses the ætiological importance of injury and inflammation, as well as the question of malignancy.

de Schweinitz gives good drawings of a papilloma growing from the plica semilunaris.

HIRSCHBERG AND BIRNBACHER.—C. f. A., viii, 1884. PARISOTTI.—Rec. d'Ophth., 1884. MAGNUS.—K. M. f. A., xxv, 1887. ELSCHNIG.—A. f. A., xix, 1889. FUCHS, S.—A. f. A., xx, 1889. RUMSCHEWITSCH.—K. M. f. A., xxix, 1891; A. f. A., xxxiv, 1898. CASPAR.—A. f. A., xxiv, 1892. SIMS.—A. of O., xxi, 1, 1892. WAGENMANN.—A. f. O., xl, 2, 1894. ZIMMERMANN.—K. M. f. A., xxxii, 1894. COGGIN.—A. of O., xxiii, 1894. JESSOP.—T. O. S., xvi, 1896. STEINER.—A. d'O., xvi, 1896. WEEKS.—New York Eye Infirmary Rep., 1896. STUELP.—C. f. A., xxi, 1897. BURNETT.—T. Am. O. S., 1897. LAGRANGE AND MAZET.—Ann. d'Oc., cxix, 1898. GRUNERT.—K. M. f. A., xxxvii, 1899. COLUCCI.—Ann. di Ott., xxviii, 2, 1899. DE SCHWEINITZ.—T. Am. O. S., 1900. *KOPETZKY V. RECHTPERG.—A. f. O., li, 1900. LAMBERT.—T. Am. O. S., 1901. ALTLAND.—A. f. A., xliv, 1901. KOERBER.—Z. f. A., x, 1903.

SIMPLE GRANULOMA

Simple granulation-tissue tumours occur frequently as the result of irritation, ulceration, or injury. They are particularly common in chalazia which have broken through the conjunctiva or have been incompletely dealt with, and in tenotomy wounds. They may be sessile or definitely polypoid.

Microscopically they are typical granulation tissue (Fig. 56), with its great variety of cells, amongst which all kinds of leucocytes, endothelial cells, giant-cells, and young connective-tissue cells are found (Figs. 57, 58). They are richly pervaded by very thin-walled new vessels, and hæmorrhages are common. It may not be easy to distinguish them from inflamed capillary nævi. They are usually un-



FIG. 56.—SIMPLE GRANULOMA OF THE CONJUNCTIVA. × 55.

The growth consists of extremely vascular tissue, partly covered by epithelium. It is made up of round and polygonal cells, many of which are epithelioid; others are lymphocytes, and there are a few polymorphonuclear leucocytes.

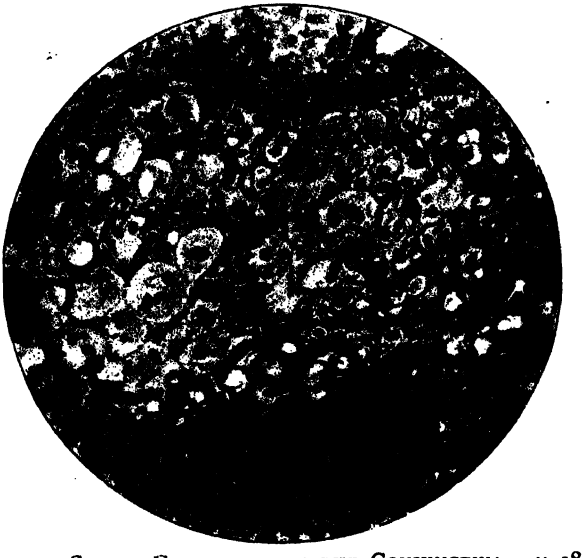


FIG. 57.—SIMPLE GRANULOMA OF THE CONJUNCTIVA. × 180.

Another part of the same specimen more highly magnified, showing very large, swollen, epithelioid cells.

covered by epithelium, but layers of rapidly growing epithelium often partially cover the peripheral parts, and islets of epithelium are often enclosed, especially near the surface (Fig. 58).

They often bleed, being a cause of "bloody tears," and they also drop off as the result of the movements of the lids.

Simple granulomata may reach a large size and project between the lids, which partially strangle the pedicle. The head is then œdematous, and the microscopical characters are not unlike those of myxomatous tissue. Moreover the epithelium covering the surface dips into every crevice of the granulation tissue, so that the appearance of epithelioma may be simulated (*cf.* case reported by Hartridge).

Granulation tissue often accumulates around embedded foreign

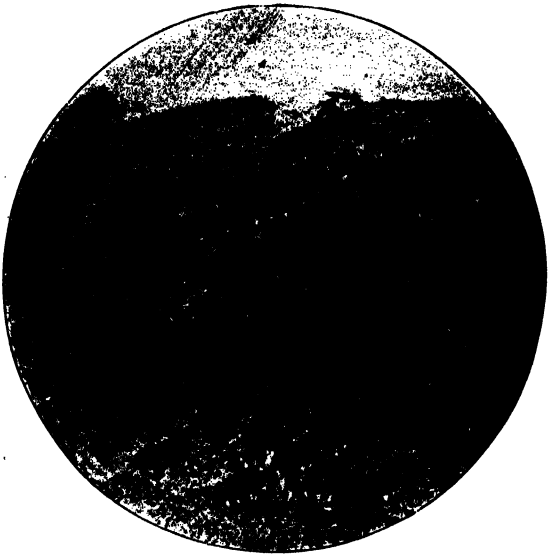


FIG. 58.—SIMPLE GRANULOMA OF THE CONJUNCTIVA. × 120.
Showing the epithelium invading every crevice of the irregular surface of the growth, passing downwards in places for a considerable distance. There are many red corpuscles and polymorphonuclear leucocytes.

bodies. One such case is reported by Uhthoff; the patient was a stonemason, and had a small growth on the conjunctiva which was taken for a melanotic sarcoma. Examination showed it to consist of granulation tissue with giant-cells, developed around quartz particles which gave an iron reaction.

HARTRIDGE.—T. O. S., xxii, 1902. UHTHOFF.—Verhandl. der Natürforscher, Nuremberg, 1893.

LYMPHOMA

Lymphomata belong to the ill-defined group of round-celled tumours, which doubtless represent very different pathological conditions (*v.* p. 18).

They occur in leukæmic and allied conditions, and consist of mononuclear round-cells embedded in wide-meshed, fine connective tissue, with relatively few vessels. They also contain numerous endothelial cells, with large faintly staining nuclei. It has been described in the plica semilunaris (Koerber).

Lymphosarcoma is not easily distinguished anatomically from simple lymphoma. It has also been described in the plica semilunaris (*v. infra*).

LEBER.—A. f. O., xxiv, 1, 1878. AXENFELD.—A. f. O., xxxvii, 4, 1891. BERL.—B. z. A., xxxvii, 1899. KOERBER.—Z. f. A., x, 1903.

FIBROMA

The typical "polypus," growing from the fornix, is usually a fibroma. It is distinguished from the papilloma in having a smooth surface, but



FIG. 59.—FIBROMA OF THE CONJUNCTIVA. × 10.

The growth was taken from a socket. Note the true papillæ on the surface. The epithelium contains goblet-cells in places.

this requires care in observation, as the moist, swollen papillæ often seem fused together. Fibromata also occur at the canthi, usually the inner, growing from the plica semilunaris. They are mostly soft, but the consistency varies with the amount and character of the fibrous tissue.

Soft fibromata grow rapidly, are very vascular, and readily bleed, both internally, giving rise to deposits of blood-pigment, and externally, causing "bloody tears." They consist of masses of fibrous tissue, chiefly arranged in longitudinal bundles (Fig. 59), covered by conjunctival epithelium of about the normal thickness. They contain many oval

and spindle-shaped young connective-tissue cells, and are often infiltrated with lymphocytes and polymorphonuclear leucocytes, which also invade the epithelium. The fibrous tissue is frequently œdematous, probably due to the pressure of the lids upon the pedicle, the tumours being often large. Hence they are sometimes described as myxofibromata, probably a misnomer (Fig. 60) (Morton). They may be covered by thickened epithelium, so that some resemblance to papilloma is brought about (Rumschewitsch).



FIG. 60.—FIBRO-MYXOMA OF PLICA SEMILUNARIS.

After Morton and Treacher Collins T. O. S., x, pl. vi). From one of the tumours, showing myxomatous structure.

Hard fibromata consist of compacter fibrous tissue, with very few connective-tissue cells and few vessels. They are also covered by rather thin epithelium, and this is often arranged upon true papillæ, the surface being smooth. They occur principally on the lid conjunctiva and on the caruncle, and do not usually recur so readily after removal as the soft form.

Fibromata were carefully described by Mackenzie, and their pathological position was determined more recently by Elschnig.

A telangiectatic fibroma from the plica semilunaris has been reported by Paderstein. It followed an injury by a twig, and consisted of soft, cellular fibrous tissue, with a hyaline capsule and hyaline deposits. It was very vascular.

MACKENZIE.—Diseases of the Eye. ELSCHNIG.—A. f. A., xix, 1889. MORTON.—T. O. S., x, 1890. ISCHREYT.—A. f. A., xxxii, 1896. RUMSCHEWITSCH.—A. f. A., xxxvi, 1898. PADERSTEIN.—A. f. A., xliii, 1901.

HÆMANGIOMA

Hæmangiomata are either *capillary* (angioma [Virchow]) or *cavernous*. They occur most commonly in children (before the twentieth year in twenty-nine cases out of forty-four [Pergens]), and are often congenital. The plica semilunaris is most affected, but they also occur in all parts.

Histologically they consist of convoluted capillaries, with very little interstitial tissue. When this is increased they are called *angiofibromata*, and all grades between these and soft fibromata occur. *Angiosarcomata* also occur, but here the sarcomatous condition is the essential feature. In some cases dilatations occur, filled with blood, forming cavernous angiomata, but these are rarer (Fig. 61). The vesse s involved may be either conjunctival, scleral, muscular, or orbital.

In twenty-one cases the distribution and nature of the angiomata were as follows :—(1) From the globe—four angiofibromata, four cavernous, one mixed ; (2) from the plica—one simple, one cavernous

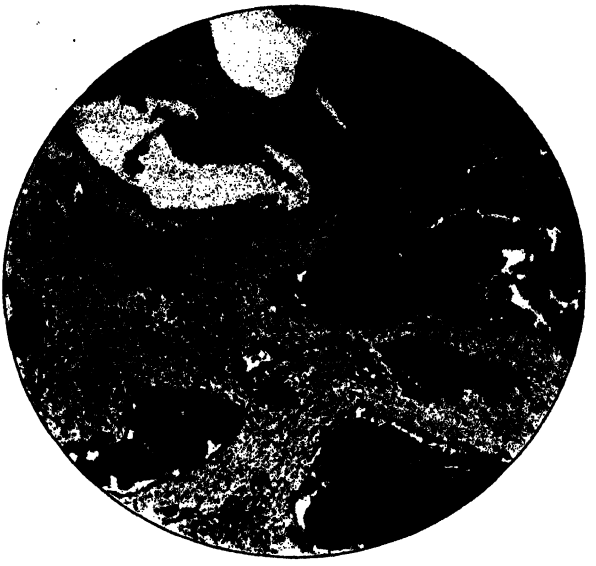


FIG. 61.—CAVERNOUS ANGIOMA. × 55.

From an encapsuled growth, the size of an almond, in the lower fornix. Large venous sinuses, lined with endothelium and filled with red corpuscles, are seen. The structure is identical with that of normal erectile tissue.

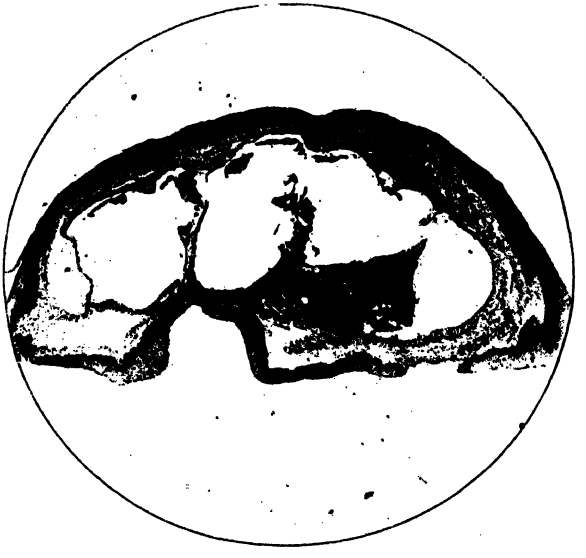


FIG. 62.—HÆMANGIOMA OR BLOOD-CYST. × 17.

The spaces are lined with endothelium and contain many red corpuscles. The dark triangular projection on the right below consists of a mass of dilated capillaries packed with red corpuscles. The epithelium over the convex surface is corneous.

(3) from the caruncle—one angiofibroma; (4) from the fornix—two cavernous angiomata, one cavernous fibro-angioma; (5) from the lid—two simple, one cavernous, one fibro-angioma, two cavernous fibro-angiomata (Pergens).

Capillary angiomata (telangiectases) vary in shape, being round or elongated, with smooth or irregular surface.

In Eversbusch's and Alt's cases numerous acinous glands were present, the plica being affected; in Reis's case, which was near the limbus, there were cystic spaces and nests of epithelium. It is possible that some are developed in pure congenital nævi. Paderstein describes a telangiectatic fibroma from the plica (*v. infra*). Parts of the same tumour may be capillary and cavernous.

Cavernous angiomata may be polypoid (Rampoldi and Steffanini, Kroschinsky), but commonly form rounded tumours, which can be partially emptied of blood by pressure and position of the body (Fig. 61). The spaces are lined with a single layer of endothelium, and are separated by a network of bands of fibrous tissue, which may be very cellular, or hyaline. They contain many wide vessels. The spaces contain masses of red corpuscles, or fibrinous coagula, or hyaline exudates. Fehr and Burnett have found calculi like those met with in varicose veins. They are seen, after decalcification, to consist of concentric layers of hyaline material, merging into fibrous tissue peripherally. Sometimes striated muscle is found in the fibrous tissue between the spaces; these angiomata probably originated in the muscle and invaded the conjunctiva secondarily.

Angiomata are usually benign; some grow rapidly, others remain stationary or commence suddenly to grow.

Telangiectatic sarcoma of the plica semilunaris has been reported by del Monte.

WARDROP.—Essays on the Morbid Anatomy of the Eye, Edinburgh, 1808; On Fungus Hæmatodes, Edinburgh, 1809. LEBER.—A. f. O., xxvi, 3, 1880. HORROCKS.—T. O. S., iii, 1883. EVERSBUSCH.—B. d. o. G., 1883. RAMPOLDI AND STEFFANINI.—Ann. di Ott., xiii, 1884. SNELL.—T. O. S., xiii, 1893. KROSCHINSKY.—B. z. A., xiv, 1894. ALT.—Amer. Jl. of O., xii, 1895. LIPPINCOTT.—T. Am. O. S., 1895. FEHR.—A. f. O., xliv, 3, 1897. BURNETT.—A. of O., xxvi, 1897. REIS.—K. M. f. A., xxxviii, 1900. *PERGENS.—K. M. f. A., xxxix, 1901. PADERSTEIN.—A. f. A., xliii, 1901. AHLSTRÖM.—B. z. A., liv, 1902.

LYMPHANGIOMA

Dilatations of the lymphatics of the conjunctiva have been studied by Steudener (1874), Imre (1876), Laskiewicz (1877), Bull (1878), Delecœuillerie (1892), and others. They occur in three forms, which cannot be dogmatically separated, viz. lymphangiectasis, lymphangioma, and lymphatic cysts.

Lymphangiectasis.—Small dilatations of the lymphatics of the conjunctiva are of common occurrence. They are rarely larger than a pin's head, are often arranged like rows of pearls, and contain clear fluid. Microscopically they resemble the dilated lymphatics found in many inflammatory conditions, *e.g.* episcleritis. The endothelium is intact, and the vessels contain granular or hyaline coagulum with a

few leucocytes. By injury they may become filled with blood, and a permanent communication with a blood-vessel may follow (*lymphectasia hæmorrhagica* [Leber]). Zimmermann has recorded such a case.

Lymphangioma.—Large cavernous dilatations of the lymphatics are rare. Uhthoff described a small unilocular cyst. More frequently there is a system of cavities, separated by thin septa (Fig. 63). These are composed of fibrous tissue and are lined by endothelium. The conjunctival stroma is pressed apart. Such cases have been reported by Alt, Jocqs, Snell, etc. Nettleship gives a good drawing of a lymphatic "nævus." I have examined a very extensive lymphangioma, in which the whole conjunctival sac was involved.

This case nearly resembles one very fully reported by Meyerhof,



FIG. 63.—LYMPHANGIOMA OF CONJUNCTIVA. × 55.

Note goblet-cells in epithelium, which is more highly magnified in Fig. 16. The adenoid layer below is infiltrated. The spaces are dilated lymph spaces, lined by endothelium; many contain hyaline material. *See* MacCallan, T. O. S., xxiii, 1903.

and the appearance of the boy was very like that shown in one of his figures. This author gives a most exhaustive bibliography of the subject.

Care must be exercised in the diagnosis of these tumours. In the case related the spaces filled with blood after the removal of a small portion for examination, and remained so filled for some weeks. Had it been examined during this period it might doubtless have been mistaken for a hæmangioma.

I have also seen a case in which conjunctival lymphangioma accompanied lymphatic dilatation of the same side of the face. The continuity of the spaces could be easily demonstrated by pressing the fluid from one part into the other.

Sourdille records a congenital lymphangioma of the conjunctiva, and the predisposing condition is probably generally present at birth, full development being gradual.

Lymphangiomata of the plica semilunaris have been reported by Vossius and Sachs.

STEUDENER.—Virchow's Archiv, lix, 1874. IMRE.—Wiener med. Woch., 1876. LASKIEWICZ.—Nagel's Jahresb., 1877. BULL.—Amer. Jl. of Ophth., 1878. DELECŒUILLERIE. —Thèse, Paris, 1892. ZIMMERMANN.—B. z. A., xxxvii, 1899. UHTHOFF.—Berl. klin. Woch., 1879. ALT.—Lectures on the Human Eye, New York, 1880. Jocqs.—Soc. franç. d'Opht., 1898. SNELL.—Brit. Med. Jl., 1898. NETTLESHIP.—T. O. S., iv, 1884. PARSONS. —In MacCallan, T. O. S., xxiii, 1903. * MEYERHOF.—K. M. f. A., xl, 1902 (Bibliography). SOURDILLE.—A. d'O., xviii, 1898. VOSSIUS.—B. d. o. G., 1887. SACHS.—Inaug. Diss., Königsberg, 1889; Ziegler's Beiträge, v, 1889.

CONGENITAL TUMOURS

Nævus.—The conjunctiva is modified skin, and like the skin, it is

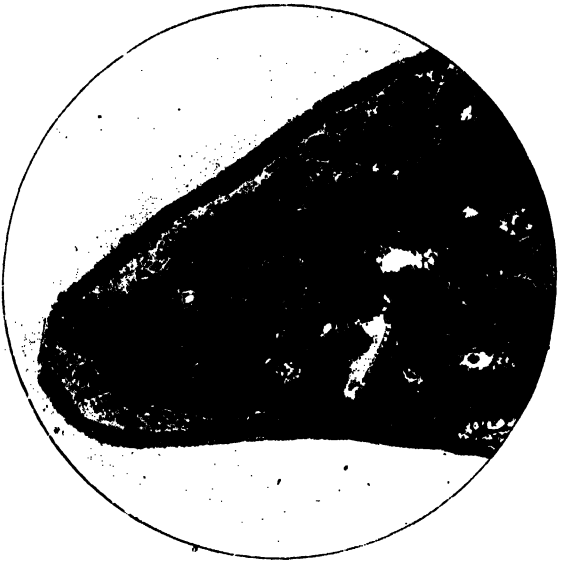


FIG. 64.—PIGMENTED NÆVUS FROM THE PLICA SEMILUNARIS. × 60.

The growth consists chiefly of "nævus cells," which are seen better in Fig. 65. Evidence of chronic conjunctivitis is seen in the slight round-celled infiltration, and in the presence of new-formed glands, lined by epithelium containing many goblet-cells. These are not uncommon in nævi of the conjunctiva. Amongst the nævus-cells are branched pigmented cells (chromatophores).

sometimes the seat of congenital growths. The commonest are nævi, dermoids, and fibro-fatty tumours.

Nævi resemble those of the skin; they are usually pigmented, rarely non-pigmented. They occur merely as grey or brown spots, or as reddish or brown flat swellings, usually at the limbus. Both types are benign, but both possess high potential capacity to become malignant.

The pignented spots are flat, and are made up of groups of large

cells of endothelial type—round or polygonal, flat, often with processes. The pigment is both intra- and inter-cellular, and consists of golden or brown granules or heaps, of various sizes. The connective-tissue cells may also be pigmented, and the epithelium over the spot also frequently contains pigment. When these spots start proliferating they form intensely malignant melanotic growths.

The more typical nævi much more nearly resemble those of the skin (Fig. 64). They are slightly swollen and gelatinous-looking, and smooth. The epithelium is prolonged downward for a short distance in club-shaped expansions, which divide and form a network. In the spaces of this network are groups of smaller epithelioid cells—the so-called "nævus cells" (Fig. 65). They have, therefore, a sort of alveolar arrangement, and are separated off from the epithelial cells



FIG. 65.—NON-PIGMENTED NÆVUS FROM THE LIMBUS. × 120.

From the limbus at the outer side. The "nævus-cells" are well seen. They are in close relationship with the superficial epithelium, though apparently independent of it. Some are arranged in an alveolar manner, others are diffuse. There are no chromatophores.

and the substantia propria by strands of fibrous tissue, which, however, forms no stroma between the cells except at the periphery of the alveoli. The nævus-cells are usually less well marked off on the deeper surface, strands of white and elastic fibres passing between them.

The nævi may be non-pigmented or pigmented. In the latter case the pigment is present throughout, but most on the surface, the epithelium also participating. The granules are brown and irregularly distributed; many of the spindle-shaped and stellate connective-tissue corpuscles are deeply pigmented, some being isolated, others forming bands. These have been called *chromatophores*.

Opinions vary as to the ontogeny of the nævus-cells. Some authors regard them as epiblastic, others as mesoblastic, and opinions again vary as to details. Many look upon them, with much probability, as endothelial cells (v. Recklinghausen); others as offspring of the chromatophores (Ribbert); others as epithelial cells which have been pinched off from the normal layers (Unna), and these, indeed, regard the chromatophores themselves as descendants of epithelial cells (Abesser). When they become malignant they are named according to the views of their origin, as alveolar sarcomata or endotheliomata, or as epitheliomata, melanomata, etc. The difficulty is exemplified in a case reported by Lawford. Leber, from a study of malignant forms, thinks the cells are epithelial. It is suggestive that they never occur isolated

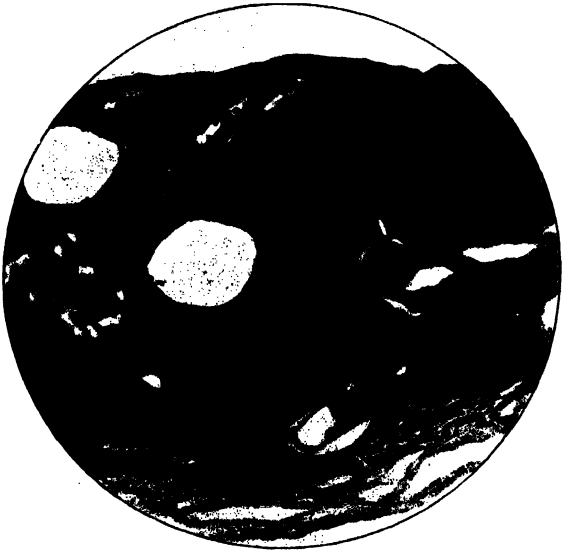


FIG. 66.—CYSTIC NÆVUS FROM THE LIMBUS. × 60.

From a specimen by Treacher Collins. The growth is composed of a mass of "nævus-cells," in which there are many round cystic spaces.

in the deeper tissues, but always in connection with the epithelial surface.

It is common to find cysts in these tumours, and the cystic development may be very pronounced (Stoewer, Pindikowski) (Fig. 66). This has been cited in favour of the endothelial origin of the cells, the tumours being really lymphomata. In Pindikowski's case the cysts were lined with a double layer of endothelium, but I have seen them as mere holes, the lining cells differing in no respect from the surrounding nævus-cells. The latter are pushed apart, and may be much reduced in numbers; their alveolar arrangement may be lost, and in some cases is absent in all parts (Best). The other school regard these cysts as due to cystic degeneration of the gland-like epithelial depressions, and the presence of numerous goblet-cells lends colour to

this view (Pindikowski). The cysts are most frequently empty in sections—evidence of their containing simply serous fluid; or they may contain coagula, with degenerated cells, or even hyaline concretions (Wintersteiner).

PARINAUD.—A. d'O., iv, 1884. RIBBERT.—Ziegler's Beiträge, xxi, 1897. UNNA.—Histopathologie der Hautkrankheiten, 1894. WAELSCH.—Arch. f. Dermatologie u. Syph., xlix. ABESSER.—Virchow's Archiv, clxvi, 1901. LAWFORD.—T. O. S., xiii, 1893. LEBER.—B. d. o. G., 1898. WINTERSTEINER.—B. d. o. G., 1898. BEST.—B. z. A., xxxvii, 1899. HIRSCH.—Z. f. A., iv, 1900. STOEWER.—A. f. O., liv, 3, 1902. PINDIKOWSKI.—A. f. A., xlii, 1901. DE SAVIGERIE.—La Clin. opht., 1900. BALLABAN.—A. f. A., xliii, 1901. ROCKLIFFE.—T. O. S., xxi, 1901. DE SCHWEINITZ AND SWEET.—Ophth. Record, 1902.

Epithelial Plaques.—Bowman, in 1853, described a "wart" which he removed from the cornea of a woman of twenty-eight. It is doubtful if this was a true wart, since it consisted of thickened epithelium.

Warlomont, in 1860, described an epithelial opacity of the lower and outer quadrant of the cornea; and Hocquard, in 1881, reported cases of epithelial proliferation. They are of two kinds. One consists



FIG. 67.—EPITHELIAL PLAQUE. × 10.

From Lister and Hancock (R. L. O. H. Rep., xv). From a man æt. 24; noticed at least ten years.

simply of local hyperplasia of the corneal and neighbouring conjunctival epithelium. The other consists of a white mass like beaten-up white of egg. It is easily removed, and is indeed continually being brushed off by the lids, so that similar masses may be found free in the lower conjunctival fornix. The epithelium undergoes fatty degeneration. It is reproduced in from three to thirty-six hours. These are simply cases of xerosis conjunctivæ (Leber) (q. v.).

Fumagalli has described a case of hyperplastic epithelial plaque, which was first considered to be a pterygium. It extended almost across the cornea, and vision was reduced to perception of light. It was easily removed, and sight was completely restored and retained. The growth consisted simply of very thick stratified epithelium, the cells of which were actively proliferating, as shown by karyokinetic figures.

Probably none of these cases are worthy of a separate designation. They are all either cases of xerosis of the conjunctiva or of epidermoid changes in the cornea, which occur under all conditions of exposure, *e. g.* lagophthalmia, etc. There is, however, a very small group of



FIG. 68.—EPITHELIAL PLAQUE. × 80.

From Lister and Hancock. Showing the superficial horny layers, stratum granulosum, and infiltration of the adenoid layer.



FIG. 69.—EPITHELIAL PLAQUE. × 80.

From Lister and Hancock. Showing the sharply defined margin of the growth. From a girl æt. 15.

cases to which the distinctive term "epithelial plaque" may be conveniently applied.

I have had the opportunity of examining two such cases. In each case they occurred in young patients and were probably congenital. In one the plaque occupied the typical position of a dermoid tumour, being partly over the cornea, out and up. In the other it was in a similar direction, but separated from the cornea by normal conjunctiva. In each case the epithelium was much thickened and the superficial layers were corneous. I think these plaques are the simplest expression



FIG. 70.—EPITHELIAL PLAQUE. × 15.

From Lister and Hancock. Showing the great hypertrophy of the epithelium. From a man æt. 51, following an injury.

of a dermoid tumour, only the epidermal elements being represented, those of the cutis vera being absent.

Hancock and Lister have recently collected cases of this type.

BOWMAN.—Ann. d'Oc., xxx, 1853. WARLOMONT.—Ann. d'Oc., xliv, 1860. HOCQUARD.—A. d'O., i, 1881. FUMAGALLI.—Arch. per le Sc. med., xvi. LEBER.—A. f. O., xxix, 3, 1883. BEST.—K. M. f. A., xxxviii, 1900. *HANCOCK AND LISTER.—R. L. O. H. Rep., xv, 4, 1903.

Dermoid.—Dermoids are lenticular yellow or reddish congenital tumours which occur astride the corneal margin, usually on the outer side, and contain the elements of skin (stratified epithelium, hairs, sebaceous glands, etc.) (Fig. 71). They were described as early as 1742, and four cases were published by Wardrop (1808); they were named "dermoids" by Ryba (1853).

While commonest at the outer part, they occur rarely at any part of the limbus, and even under the outer canthus, etc. Examples are given by Vassaux. They are often associated with other congenital malformations (twenty-seven out of ninety-four [Picqué]), "colobomata" of the lids, fleshy bands from the globe to the face, etc. They occur in lower animals (*cf.* Oeller), and have wool instead of hairs in the sheep (Museum, R. C. S.) (Bland-Sutton). They rarely start growing until puberty, and it is then that the hairs develop. They may be as small as a pin's head, or so large as to project between the lids. The base is generally oval, with the long axis horizontal, and they are

nearly flat, but may be rarely pedunculated (Snell) (Fig. 73). When there is a notch in the lid the tumour corresponds in position with the gap. They usually have few or no vessels, and are hard—rarely soft. They are sometimes covered with sebaceous secretion (Vassaux, van Duyse).

The epithelium has all the characteristics of true epidermis, possessing a superficial horny layer, stratum lucidum, stratum granulosum, and Malpighian layer of prickle-cells.

The corium consists of fibrous tissue, with many elastic fibres, and a few vessels. The papillæ are usually ill-developed. Pigmented spots have been found in the superficial layers (Vassaux). The deeper layers are areolar, the fibres being more loosely set, and containing fat, which



FIG. 71.—DERMOID OF THE CONJUNCTIVA.

Argyll-Robertson (T. O. S., xiv). Note the hairs upon the surface. The position is as usual, up and out, but is unusually far from the cornea.

may be conspicuously developed and form a connecting link with the fibro-fatty tumours. In the deepest part the fibres are continuous with those of the sclerotic, so that the tumour is immovable upon the eye; rarely it is movable. Nearly all dermoids contain hairs with well-developed follicles and sebaceous glands. Sweat-glands are rare, but have been found (Heyfelder, Vassaux, Gallenga) (Fig. 73); some are more nearly allied to Moll's modified sweat-glands. Medullated nerves have been found in the deep layers (Vassaux), and in a fleshy band (Poncet) which has exactly the same structure (Manz, Nuel, Lannelongue, van Duyse, Poncet). Dermoids rarely contain cartilage (Gallenga).

Various theories have been suggested for the explanation of dermoids. Ryba suggested failure of complete closure of the lids,



FIG. 72.—DERMOID OF THE LIMBUS. × 55.

From a boy æt. 3; it was situated astride the limbus, *down* and out. It consists chiefly of hyaline connective tissue with a few small blood-vessels covered by epidermis, which is horny on the surface in places. The section shows a hair-follicle and sebaceous gland.

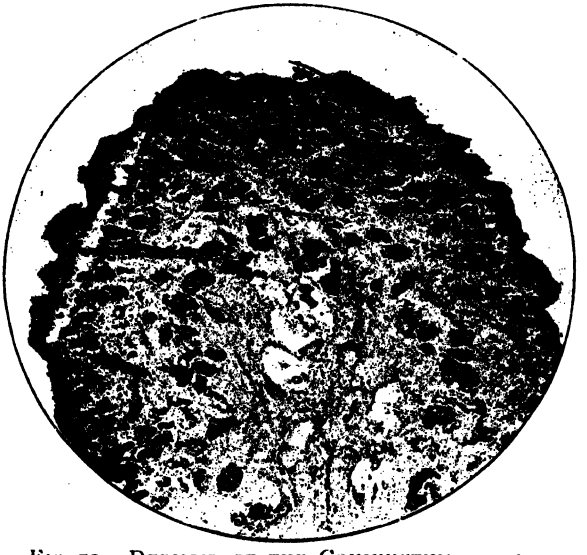


FIG. 73.—DERMOID OF THE CONJUNCTIVA. × 20.

From the case reported by Snell and Treacher Collins (T. O. S., xx). Pedunculated dermoid from upper and outer part of conjunctiva of a boy æt. 5 months. Note the enormous number of sweat-glands. There were a few hair-follicles in the terminal part, and several sebaceous glands in the pedicle.

with consequent cornification of the conjunctiva, and cited the correspondence of dermoid and lid-notch. This view is supported by Bland-Sutton and Treacher Collins; the latter regards cryptophthalmia, in which the whole surface of the eyeball is covered with skin, as the ultimate manifestation of dermoid development. Gallenga drew attention to the plica semilunaris, which in fœtal life covers the globe, like its phylogenetic equivalent the nictitating membrane. He thought it might remain adherent to the limbus. Osborn thought the tumour might be a remnant of the epiblast which forms the lens. van Duyse considered it was due to adhesion of the amnion to the eye. This theory has been held in modified form by Lannelongue and Vassaux.

The eye is usually otherwise normal, but there is a group of cases in which it is congenitally deformed. Such cases are described by Schmidt-Rimpler, Swanzy, Bernheimer, Manfredi, Wagenmann, etc. In Wagenmann's case there was bone in the dermoid or teratoid tumour.

Sweat-glands were present in Swanzy's case, and besides those mentioned there is a group in which similar serous acinotubular glands are present, with much fatty tissue, striped and unstriped muscle-fibres, hyaline bodies, bone, and nerves. They are covered by conjunctival epithelium with goblet-cells, and form a further link towards the fibro-fatty and more purely orbital teratoid growths. They are supposed to represent the fornix area, the glands being Krause's glands (Falchi). When these growths are combined with dermal tissues, Gallenga supposes that the dermoid leads to the malposition of Krause's glands by being intruded into the normal tissues; but it must be remembered that Krause's glands are inconstant in position.

The epithelium even in ordinary dermoids is not always epidermal, but may be conjunctival, especially when the growth is covered by the lids. If it projects between the lids the exposed part becomes horny, but this is the case in many other pathological conditions, *e. g.* anterior staphyloma, etc.

WARDROP.—Essays on the Morbid Anatomy of the Eye, Edinburgh, 1808. RYBA.—Prager Vierteljahresschrift, iii, 1853. VASSAUX.—A. d'O., iii, 1883. PICQUÉ.—Thèse, Paris, 1886. OELLER.—A. f. A., x, 1881. BLAND-SUTTON.—Tumours, London. TREACHER COLLINS.—Lancet, 1900. SNELL.—T. O. S., xx, 1900. VAN DUYSE.—Ann. de la Soc. méd. de Gand, 1882. VAN DUYSE AND BRIBOSIA.—A. d'O., xv, 1895. GALLENGA.—Ann. d'Oc., xciv, 1885; Ann. di Ott., xxviii, 1899. HEYFELDER.—In Fuchs, K. M. f. A., xviii, 1880. PONCET.—Bull. de la Soc. de Chir., iv, 1883. MANZ.—A. f. O., xiv, 2, 1868. LANNELONGUE AND ACHARD.—Traité des Kystes congénitaux, Paris, 1886. OSBORN.—St. Thomas's Hosp. Rep., vi, 1875. SCHMIDT-RIMPLER.—A. f. O., xxiii, 4, 1877. SWANZY.—Dublin Quarterly Jl. of Med. Sc., 1871. BERNHEIMER.—A. f. A., xviii, 1888. MANFREDI.—Riv. Clin., v, 1869. WAGENMANN.—A. f. O., xxxv, 3, 1889. FALCHI.—A. f. A., xl, 1900.

Dermo-lipoma.—Fibro-fatty tumours of congenital origin are found usually in the same situation as dermoids, at the outer margin of the cornea, or farther out, between the insertions of the superior and external recti. The conjunctiva is generally thickened. They are usually yellow, about the size of a pea or bean.

Microscopically they consist of fatty tissue with irregular strands of fibrous tissue (Fig. 74). They were at first described as ordinary lipomata, the earliest being recorded by Kranke (1854). Some, *e. g.*

Querenghi's, may indeed be simple lipomata. Reuss, in 1891, could only collect twenty cases. After that they increased in interest, owing to the discovery of other tissues. Talko found glandular tissue and hyaline cartilage (lipo-chondro-adenoma bulbi). Other observers found elements of skin, as in the ordinary dermoids. Rieke insisted upon the necessity of extremely careful examination, as the cutaneous elements may be limited to a single stunted hair-follicle or sebaceous gland, so that it is sometimes necessary to make serial sections. A very careful investigation of four cases from this point of view was carried out by Nobbe, under the supervision of Leber. In all cases hairs and sebaceous glands were found, and in one an accessory lacrymal gland, in another smooth and striped muscle-fibres. Rogman, on the other hand, failed to find dermal elements in one of five tumours examined,



FIG. 74.—DERMO-LIPOMA. × 7.

From a child æt. 1 year. The tumour consists of fibrous and adipose tissue, covered by conjunctiva. Near the edge below acini of lacrymal gland are seen.

so that their teratoid nature cannot in all cases be demonstrated. This is confirmed by one of Lagrange's three cases. Fibro-fatty tumours have also been recorded by Derby, Bögel, Würdemann, Alt, Weyman, Marcus Gunn, etc. Other transition forms from true dermoids have been already alluded to (*v.* p. 133). The true dermoid described by Hirschberg and Birnbacher, occurring in the equatorial region, is interesting as showing that these growths are not limited to the limbus and the caruncle.

The tumours are always congenital, but are often not noticed at once owing to their position up and out, under the upper lid, and also owing to the fact that, like dermoids, they may start growing at puberty; but this is less common with the lipo-dermoids. They have

been described mostly in girls. They are essentially conjunctival, and not orbital growths, as held by von Graefe. The same theories are said to account for them as for dermoids, but the occurrence of simple lipomata cannot be eliminated. Lagrange considers that the conjunctiva moves freely over lipomata, but is adherent to dermo-lipomata.

KRANKE.—Ann. d'Oc., xxxi, 1854. DERBY.—T. Amer. O. S., 1878. BÖGEL.—A. f. O., xxxii, 1, 1886. TALKO.—K. M. f. A., xxvi, 1888. RIEKE.—A. f. A., xxii, 1890. REUSS.—C. f. A., xv, 1891. *NOBBE.—A. f. O., xliv, 1897. ROGMAN.—Ann. d'Oc., cxix, 1898. *LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. WÜRDEMANN.—Amer. Jl. of Ophth., 1888. ALT.—Amer. Jl. of Ophth., 1889. WEYMAN.—Ophth. Rec., 1892. MARCUS GUNN.—Ophth. Rev., 1889. HIRSCHBERG AND BIRNBACHER.—C. f. A., vii, 1883.

Osteoma.—Osteomata of the conjunctiva have been observed by v. Graefe (1863), Saemisch, de Wecker, Anderson Critchett, Spencer



FIG. 75.—OSTEOMA OF THE CONJUNCTIVA. × 55.
From a girl æt. 14; lying upon the sclerotic external to the cornea; adherent to globe, but not to conjunctiva. It consists of true bone; there is no cartilage.

Watson, Shadford Walker, Loring, Snell, Vignes, Galtier, Cirincione, Hartridge, and Heustis. I have myself examined three such tumours from different patients. They are therefore not so rare as might be thought.

They always occur in the upper and outer quadrant, between the tendons of the superior and external recti; they are always congenital. They may be definitely classified amongst the teratomata, and are probably examples of atavism, a reversion to the types in which plaques of bone are found in the skin. They have nothing to do with the plaques of bone found in the sclerotic of birds, etc., since they are always in the conjunctival stroma, and are movable over the normal sclerotic. They have been explained on the same theory as dermoids (q. v.).

The tumour is usually convex on the upper and flattened on the deep surface. It is surrounded by periosteum, which is embedded in the

substantia propria of the conjunctiva. The bone is usually irregularly developed, the laminæ running in all directions (Fig. 75). They are roughly arranged in Haversian systems around the thin-walled vessels, and have numerous typical bone-corpuscles. None of mine contained cartilage, but they often do.

v. Graefe.—K. M. f. A., i, 1863. Saemisch.—In de Wecker, Traité d'Opht., i, p. 426, 1880. de Wecker.—Traité d'Opht., i, p. 427, 1880. Anderson Critchett.—T. O. S., ii, 1882. Spencer Watson.—Brit. Med. Jl., 1882. Shadford Walker.—Brit. Med. Jl., 1882. Loring.—New York Med. Jl., 1883. Snell.—T. O. S., iv, 1884. Vignes.—Soc. franç. d'Opht., 1889. Galtier.—Ann. d'Oc., cxiii, 1895. Cirincione.—Lav. d. Clin. Oc. di Napoli, iv, 1895. Hartridge.—T. O. S., xv, 1895. Heustis.—Ann. of Ophth., viii, 1899. Contino.—Clin. Oculistica, 1900.

Adenoma

Adenoma of the conjunctiva can only occur where there are true glands. They are found in the caruncle (q. v.); others have been described growing from Krause's glands (Moauro, Rumschewitsch, Salzmann) (*v.* p. 27). One occurred in a man of thirty-four, and consisted of gland-lobules of ordinary type, with interlobular tissue consisting of typical granulation tissue (*adeno-granuloma*). The upper part was chiefly glandular, the lower granulation tissue. Another occurred in a girl of nine; the growth was 3 cm. long by 1·5 cm. broad by 1 cm. thick, and was in the outer part of the upper fornix. It consisted of gland-lobules with dilated spaces (cysts) in the upper and lower parts. There was a considerable amount of fibrous tissue between the lobules (fibro-adenoma cystoideum) (Rumschewitsch).

Moauro.—Riv. internaz. di Med. e Chir., iv, Napoli, 1887. Rumschewitsch.—K. M. f. A., xxviii, 1890; xl, 1902. Salzmann.—A. f. A., xxii, 1891. Schirmer.—A. f. O., xxxviii, 1, 1891.

Sarcoma

Sarcoma of the conjunctiva occurs most commonly at the limbus as an epibulbar growth (Fig. 76). The first case in which it can be isolated from the general description of "cancer" of the conjunctiva was reported by Baumgarten in 1852. Since then over eighty cases have been recorded, but this gives little idea of its relative frequency.

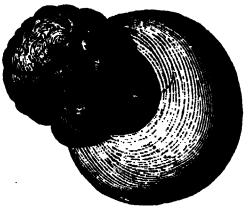


Fig. 76.—Sarcoma of the Limbus.
After Lawson.

Epibulbar sarcomata arise in the conjunctiva at or very near the limbus, especially in the more exposed parts, *i. e.* in the palpebral aperture (Panas). Several cases have occurred in which they were multiple at the limbus, and after removal they may recur at some other spot in this situation. They are usually pigmented, but non-pigmented sarcomata also occur (12 to 61), and recurrent tumours are sometimes non-pigmented when the primary growth was pigmented, and *vice versâ* (Weinbaum). Metastatic deposits from melanotic sarcomata may be non-pigmented, as in the case of the choroid, etc. Pigmented connective-tissue cells are sometimes found at the corneal

margin, and may form aggregates (melanomata [Virchow]); these are always present in dark races. They often form the starting-point of malignant growths. Such growths are sarcomata, and must be distinguished from malignant growths originating in congenital nævi, which must now probably be regarded as carcinomata (*v.* p. 127). Confusion arises from the application of the term melanoma to both types when they are pigmented.

The tumours may appear as black, brown, or red smooth round elevations or nodular masses, often friable and bleeding readily. They are at first movable with the conjunctiva over the sclerotic. The base is nearly always small, even when the growths are large, so that they often lie over the cornea without being adherent to it—a point of distinction from epithelioma. In one case the pedicle was 1·5 cm. long (Bloch); but the tumour may be a diffuse flat swelling. The corneal stroma is not usually invaded, or at most in the superficial layers only. In Wadsworth and Verhoeff's case the anterior third was infiltrated, and the whole cornea may be involved in late stages (Sgrosso). Increase in growth takes place principally in the conjunctiva, so that the tumour can still be moved over the globe. The largest was the size of an orange, and was entirely extra-bulbar (Adamück). Accounts show that they take about a year to become the size of a pea or bean. Sgrosso, Green and Ewing, and Lagrange report cases where the patient had noticed a small spot thirty, twenty-five, and fifteen years respectively, which finally underwent sudden growth and extension. A small tumour may rarely be accompanied by wide-spread pigmentation of the conjunctiva (Greeff).

The patients are usually old, but Krautner, Benson, and Schultze report cases at eight, eleven, and fourteen years respectively. The average is fifty-one. There is a history of injury in six cases, and occasionally pterygium (Strouse).

The general opinion as to malignancy is voiced by Strouse, who says that epibulbar sarcomata never penetrate the globe, and rarely produce metastases. Verhoeff and Loring regard them as highly malignant, judging by their tendency to recur and form metastases. They give the following results:

Total primary abscissions		53
No recurrence:		
After 6 months' observation	1	
„ 1 year's „	4	
„ 2 „ „	1	
„ several (4 and 10) years' observation	2	
	—	8
Recurrence:		
Within 1 year	10	
„ 2 years	3	
„ several years (4, 6, 10, 6)	4	
Time not stated	19	
	—	36
Not followed after operation		9
		53

Of the thirty-six cases with recurrence, metastasis occurred in eight, and recurrence in lids and orbit in four others. These results and further analysis of the cases would seem to show that the general opinion is wrong, and that the growths are extremely malignant, and should be treated by radical methods (primary enucleation).

Microscopically sarcomata of the limbus show few peculiarities. They are usually round- or spindle-celled, the cells being of various sizes in different cases, and generally arranged in bundles.

Multinuclear cells may also occur in them (Wadsworth and Verhoeff). These are not true giant-cells, like those found in myeloid sarcoma, but are probably merely evidence of the rapid cell-division which is going on, nuclear division proceeding more rapidly than that of the cells.

Still more commonly, however, they have an alveolar arrangement, rings and columns of cells being enclosed in fibrous-tissue framework. These alveolar sarcomata probably arise in pigmented or non-pigmented nævi. This peculiarity in structure has led Panas to doubt the frequency of sarcomata at the limbus. He thinks that they are commonly multiple, and arise at some distance from the limbus (peribulbar). The strictly epibulbar (limbus) tumours he regards as mixed epithelioma and sarcoma, and as non-malignant. This revolutionary idea cannot be held. These growths belong to a well-known type described by Virchow as sarcoma carcinomatoides, and most often called alveolar sarcoma in England.

Their nomenclature depends upon the nature of the nævus-cells from which they arise, and this, as we have seen (*v.* p. 129), is a matter of dispute. If we regard the mother cells as endothelial, these growths are endotheliomata. In any case endotheliomata probably occur in the limbus, derived from the endothelium of the blood-vessels or lymphatics (*see* "Cornea"). If nævus-cells are regarded as epithelial, in accordance with an increasing consensus of opinion, the growths are epitheliomata or carcinomata. The question of nomenclature is perhaps of little importance, but the mixture of ideas involved in asserting the simultaneous occurrence of carcinoma and sarcoma (Panas) is to be avoided.

Cases of this type have been described by Schultze (two), de Lapersonne and Curtis (one), and Panas (five), but they really form an unusually large proportion of sarcomata in this region. The epithelioid cells are said by some not to be connected with the superficial epithelium, though they often appear to be so. The epithelium passes unchanged or thinned over the surface; but it is not unusual to see "alveoli" of the cells embedded in and encroaching upon the epithelium, a condition very reminiscent of congenital moles. There are often polynuclear leucocytes between the sarcoma cells.

The pigment in these tumours may be purely intra-cellular, or may be also between the cells. Masses of granules may also be found in the vessels, or in obliterated vessels, or within fusiform cells near the vessels (Birnbacher). Different views are held as to its origin in these and other melanotic sarcomata—whether developed by the tissue cells (autochthonous) or from hæmoglobin (hæmatogenous).

The question will be discussed more fully in dealing with sarcoma of the choroid.

Whilst penetration of the globe in these cases is extremely rare, it sometimes occurs (Kerschbaumer); the growth then passes along the perforating anterior ciliary vessels. In one case sarcomatous cells were found in the canal of Schlemm. The intra-ocular invasion is never extensive. Invasion of the cornea is always at first between Bowman's membrane and the epithelium.

Sarcoma in other parts of the conjunctiva is very rare. One case has been published in which it occurred in the upper fornix (Griffith). In another it arose at the inner angle in the socket of an enucleated eye (Gorecki).

Cases of sarcoma of the palpebral conjunctiva have been published by Mittendorf, Ewetzki, and Feilchenfeld. They are sometimes pedunculated. The first was in a woman æt. 46; there were repeated small recurrent tumours: the pre-auricular and cervical glands were swollen. The second was a melanotic sarcoma in the conjunctiva of the lower lid of a man æt. 53; it consisted of round and oval cells; there were two isolated pigmented nævi on the border of the lid. The third case was a round-celled, non-pigmented growth between the tarsus and the conjunctiva, and invading the tarsus, Meibomian glands, and Riolan's muscle.

Melanotic sarcomata of the plica semilunaris have been published by Pflüger (in a man æt. 39—recurred), Rumschewitsch (in a man æt. 22—alveolar—recurred and caused death), Meighan, and de Berardinis. Lympho-sarcomata have been reported by Piccoli and Vollaro. They had the structure of adenoid tissue, and there were giant-cells in the second case.

*Lagrange.—Tumeurs de l'Œil, i, Paris, 1901 (Bibliography). *Verhoeff and Loring.—A. of O., xxxii, 1903 (Bibliography). Baumgarten.—Arch. f. Heilk., xvi, 1852. Panas.—A. d'O., xxii, 1902. Weinbaum.—A. f. O., xxxvii, 1, 1891. Wadsworth and Verhoeff.—T. Am. O. S., 1901. Sgrosso.—Ann. di Ott., xxi, 1, 1892. Adamück.—A. f. A., xi, 1881. Greeff.—In Orth, Lehrbuch, Berlin, 1902. Krautner.—K. M. f. A., xxxviii, 1900. Benson.—Ophth. Rev., vi, 1887. Schultze.—K. M. f. A., xxxii, 1894. Strouse.—A. of O., xxvi, 1, 1897. de Lapersonne and Curtis.—A. d'O., xvii, 1897. Birnbacher.—C. f. A., viii, 1884. Lawford.—R. L. O. H. Rep., xii, 3, 1889; T. O. S., xvi, 1897; xxi, 1901. Kerschbaumer.—Das Sarkom des Auges, Wiesbaden, 1900. Griffith.—T. O. S., xx, 1900. Gorecki.—Soc. franç. d'Opht., 1892. Mittendorf.—Amer. Jl. of Ophth., 1886. Ewetzki.—Nagel's Jahresb., 1886. Feilchenfeld.—C. f. A., xii, 1888. Pflüger.—Univ. Augenheilklinik Bericht, 1883. Rumschewitsch.—K. M. f. A., xxix, 1891. Meighan.—Glasgow Med. Jl., xxxviii. de Berardinis.—Ann. di Ott., xxxi, 1902. Piccoli.—Lav. della Clin. Oc. di Napoli, iv, 1895. Vollaro.—Ann. di Ott., xxviii, 1899.

Epithelioma

Epithelioma occurs *par excellence* where one kind of epithelium passes into another, as at the anus, lips, edge of lids, etc. So, too, in the conjunctiva it occurs at the edge of the lids (p. 21) and at the limbus (Fig. 77). Here it is commonly at the outer side (Panas), but it also occurs in other parts, and when it starts at a distance from the edge of the cornea it is often on the nasal side (Lagrange). It is usually

papillary or wart-like at first, about the size of a small pea, but it may grow to an enormous size and project as a fungating mass between the lids. It may much resemble a dermoid at first, but later it spreads out, covering the cornea and sclerotic, though its attachment to the globe may be small. It may simply cover the cornea, only involving the epithelium, but this is rarer than with the epibulbar sarcomata. It generally infiltrates the substantia propria of the cornea widely. It is almost invariably single, but Manz records a case with four nodules. The surface in late stages ulcerates, and small hæmorrhages take place, the blood-pigment becoming almost black, but true pigmentation may also be present. A sero-purulent exudate may occur from irritation. Lagrange regards implication of the lymphatic glands as rare, but it certainly occurs, the pre-auricular first and the submaxillary glands later being affected. The growth extends widely over the sclerotic (Figs. 78, 79), and in rare cases surrounds the cornea (*peribulbar epithelioma* [Heyder]).



FIG. 77.—EPITHELIOMA OF LIMBUS.
After Lawson. From the Museum of the R. L. O. H

Recurrence after local removal is common. Trousseau records six cases where this treatment was successful, but I think that cases of simple epithelial hyperplasia occur in which masses of epithelium are formed, much resembling those found in epithelioma. In the small piece which is excised for pathological examination the knife often fails to pass below the epithelium, so that it is impossible to determine its relations to the underlying connective tissue. These

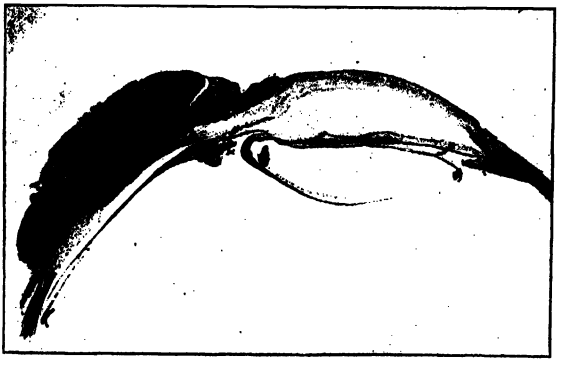


FIG. 78.—EPITHELIOMA OF THE LIMBUS. × 6.
The growth is lens-shaped, and consists almost entirely of epithelium. Bowman's membrane is curled up at the advancing edge. There is dense round-celled infiltration at the base.

tumours sometimes show no tendency to rapid growth, remaining unchanged for a considerable period. There is no question that such cases should be watched with extreme care. The malignancy seems to vary irrespective of the microscopical varieties of the growth.

Microscopically, epithelioma of the conjunctiva differs little from that of other parts (Fig. 80). The surface epithelium grows down in columns into the stroma, and these columns divide and anastomose, forming a complex coarse network, separated from each other by a variable but usually small amount of fibrous tissue carrying blood-vessels. In parts the basement membrane is broken through, and the cells shade off into the stroma, so that in this transition zone cells occur which cannot be dogmatically diagnosed as either epidermal or mesodermal, but partake of the nature of each. The peripheral cells of the bands correspond to the basal and youngest cells, and are mostly cubical or cylindrical. Upon these follow larger polygonal cells with interlocking processes, showing often beautiful examples of prickle-



FIG. 79.—EPITHELIOMA OF THE LIMBUS. × 3.

From a specimen sent by Professor Fuchs. The lid, fornix, and part of the eye are seen. The growth is entirely epibulbar, and is infiltrating the fornix and Tenon's capsule.

cells. Centrally the cells are flattened, and form epithelial pearls or cell-nests, the nuclei disappearing and the cells becoming flattened and horny. The whole is often pervaded by polymorphonuclear leucocytes, and a dense round-celled infiltration often marks the limiting zone of the stroma, giving testimony of inflammatory reaction.

The nuclei of most of the cells vary enormously. Some are small, with little chromatin; others are gigantic, rich in chromatin which is arranged in irregular lumps (Fig. 80). In many cells the nuclei are broken up; others are in active karyokinesis, which is often atypical, with an odd number of centrosomes, irregularly and unequally arranged. In some cells the nuclei are being extruded. Many present appearances suggestive of coccidia, and are considered by some, on insufficient



FIG. 80.—EPITHELIOMA OF THE LIMBUS. × 90.

To show the extraordinary variety of nuclear forms. This figure should be compared with Fig. 81, which is magnified to the same degree.



FIG. 81.—PAPILLOMA OF THE CONJUNCTIVA. × 90.

Part of Fig. 55 more highly magnified, to show the nature of the epithelium. The stroma is infiltrated with round-cells, some of which have penetrated between the epithelial cells.

grounds, to be in reality parasitic organisms. The cells therefore show much more atypical variation than those found in papillomata (Fig. 81). Here cell-division results in great hyperplasia, but the resultant cells are of almost normal type.

The corneal epithelium usually passes on to the growth unchanged. This is especially the case with the superficial layers, whilst the middle layers broaden out and become ten or twenty layers thick. The conjunctival epithelium also passes gradually into the tumour, and here goblet-cells are often present in large numbers. The cornea is invaded by the columns of tumour cells, which may lift up Bowman's membrane with the epithelium, so that these pass for some distance on to the growth. Deeper, fine columns of epithelial cells

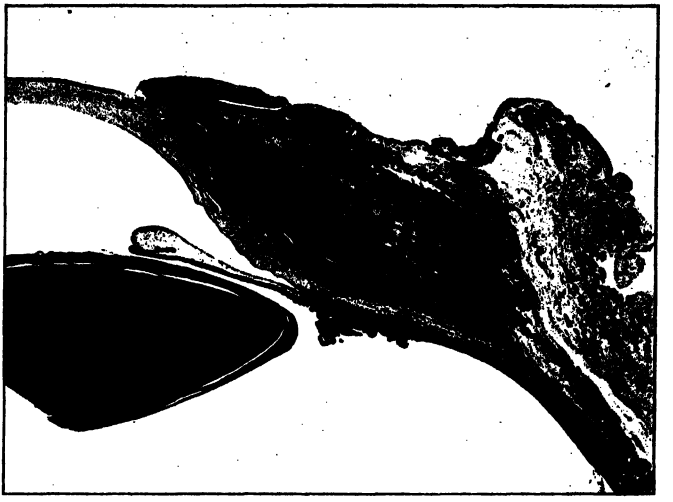


FIG. 82.—EPITHELIOMA OF THE LIMBUS. × 8.

From a man æt. 62. The spindle-shaped mass is composed almost entirely of fibrous tissue, containing, however, narrow cords of epithelial cells one or two cells deep.

invade the substantia propria, pushing the lamellæ apart and breaking them up. Posteriorly, the whole episclera is gradually invaded, and tubules now dip down in the lymph-spaces between the scleral laminæ, though apparently against great resistance. Sections, however, often show islets of epithelial cells embedded in the sclerotic, mostly in the superficial layers of the anterior part. The growth may invade Tenon's capsule, or extend into the fornix and lid (Fig. 79).

In some cases there is an enormous increase of fibrous tissue and round-celled infiltration between the corneal and scleral lamellæ, whilst the epithelial cells are few in number and form small islets or chains in the lymph-spaces (Fig. 82).

When the globe is invaded it is along the perivascular and perineural lymph-spaces of the corneo-scleral junction,—never elsewhere. This is

characteristic of all growths in this situation; it is the weak spot of the eye, and whilst epibulbar sarcomata rarely penetrate the globe, the epitheliomata do so more frequently. It is here, too, that intra-bulbar growths commonly become extra-ocular. The epithelial cells are chiefly arranged around the perforating vessels, and cling to them so that they reach Schlemm's canal, which they also surround. Usually the intima and endothelium of the vessels are intact, but intra-vascular epithelial plugs are also seen. In this manner the angle of the anterior chamber is reached, and the growth now infiltrates the intra-ocular structures. Cells may become separated from the main mass in the anterior chamber, as in other lymph-spaces, and carried to other parts, thus setting up new foci, which are in reality metastases (*cf.* v. Michel).

Epitheliomata of the conjunctiva are not infrequently pigmented, Panas considering nearly all these melanotic growths as of epithelial origin (*v.* p. 140). The epitheliomata are not usually so deeply pigmented as the sarcomata. This is explained for the hæmatogenous pigmentation by the greater rarity of hæmorrhages, due to fewer vessels, which have normal walls. In the typical melanomata the pigment is autochthonous, and the cells are doubtless offspring of the pigmented cells which often occur normally at the limbus.

Peribulbar epitheliomata have been described by Heyder (two cases), Lagrange (one case), and Reis (one case). In Lagrange's case the globe was wholly embedded in the tumour, except part of the cornea. The growth consisted of epithelial cells, not arranged typically as an epithelioma or as a carcinoma. There were no cell-nests. It is possible that all these tumours were really endotheliomata.

Epithelioma of the conjunctiva, as well as papilloma, occurs as part of the general carcinomatosis found in xeroderma pigmentosum (Greeff).

VON GRAEFE.—A. f. O., vii, 2, 1860. MANZ.—A. f. O., xvii, 2, 1878. NOYES.—T. Amer. O. S., 1882. SGROSSO.—Ann. di Ott., xxi, 1892. *LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. *HEYDER.—A. f. A., xvii, 1887. PARISOTTI.—Rec. d'Ophth., 1885. OLIVER.—A. of O., xxvi, 1897. TROUSSEAU.—A. d'O., xvi, 1896. ANDERSON CRITCHETT AND JULER.—T. O. S., xi, 1891. ALTLAND.—A. f. A., xliv, 1901. SNELL.—T. O. S., xxi, 1901. REIS.—K. M. f. A., xli, 1903.

THE CARUNCLE

INFLAMMATION

The caruncle may be inflamed with the conjunctiva; in trachoma *follicles* may develop in it. The sebaceous glands in it may be affected with diseases common to them elsewhere, *e.g.* acne; and *concretions* may form in them from retained secretion becoming impregnated with calcium salts. Thickening of the caruncle may occur in syphilis.

TUMOURS

Papillomata are the commonest tumours found here. They re-

semble those of the conjunctiva, and often show their origin by the presence of sebaceous glands in the base (Fig. 55).

Lymphangioma has the same characters as in the conjunctiva (Sachs).

Adenomata occur in young people as pink firm tumours. They may be polypoid or sessile, and grow very slowly. They are often cystic (*cystadenomata*). Cases have been described by Testelin and Prudden; those of Fontan and Schirmer apparently originated in the plica, and therefore from vestigial glands. The tubules and cysts are lined by a single layer of cylindrical epithelium, and seem to be derived from the acino-tubular glands (sweat-glands).

Nævus of the caruncle resembles that of the conjunctiva. Ginsberg describes a tumour supposed to be derived from a nævus. It was composed of infiltrated fibrous tissue, with many endothelioid cells resembling nævus cells, and was covered by epithelium which sent processes downwards into the stroma. Nævi are here particularly exposed to irritation, and, according to Wintersteiner, malignant growths develop in them much more frequently than in those of the C. tarsi.

Dermoids of the caruncle have been described by Demours, Schiess-Gemuseus, Wallenberg, Wolff, and Bock. The first three were in the plica, the caruncle being seen at the inner border. In Bock's case the tumour consisted of dense fibrous tissue, with fat, elastic tissue, medullated nerves, unstriped muscle, and sebaceous glands. A few hairs were present. The epithelium was partly a single layer of cylindrical, and partly two or three layers of large cubical cells, with many goblet-cells. This tumour may have been a mere hyperplasia or fibro-lipoma, as described by the author. There is therefore no indisputable case of dermoid published.

Cysts, apart from those found in adenomata, have been found in the caruncle and its neighbourhood by Rumschewitsch, as the result of inflammatory processes, *e.g.* trachoma. They are retention cysts occurring in the modified sweat-glands. They are multilocular, lined by a single or double layer of epithelium, having the usual characteristics of such cysts of the conjunctiva.

Epithelioma has been described by Despagnet and de Schweinitz.

Sarcoma, pigmented or non-pigmented, is the commonest malignant tumour (Veasey, Snell, de Berardinis). It is usually small round-celled, and telangiectatic fibro-sarcomata occur (del Monte, Manthey).

Carcinoma is rarer, and springs from the glands present.

Rodent ulcer apparently only occurs by extension from the lid, and in this form frequently.

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CHAPTER III

THE CORNEA

THE NORMAL CORNEA

THE cornea is the anterior portion of the coats of the eyeball, which are here specially differentiated for the transmission and refraction of light rays. The conjunctiva is reduced to a layer of stratified epithelium; the sclerotic is represented by the substantia propria, of which Bowman's membrane is merely the anterior layer, and the uveal tract persists as a single layer of endothelial cells, together with the elastic membrane (Descemet's membrane) which is derived from them. This view, which was emphasised by Schwalbe, is proved conclusively by embryological investigations (Kessler, Kölliker). At the same time, it must be admitted that there is some variation in different animals, so that Waldeyer regarded only the central lamellæ of the cornea as belonging to the sclerotic, the anterior lamellæ, with Bowman's membrane and the epithelium belonging to the conjunctiva, and the posterior lamellæ, with Descemet's membrane and the endothelium, to the uveal tract.

The cornea, viewed from in front, is horizontally elliptical; viewed from behind it is circular. This is due to the fact that it is set in the sclerotic like a watch-glass in its rim, and the sclera and conjunctiva both spread farther over the cornea above and below.

The early fœtal cornea is indistinguishable from the sclerotic, both consisting of oblong connective-tissue cells with little intra-cellular substance. It is vascular until the fifth month, after which the vessels atrophy. In its fœtal state it is not only relatively, but absolutely thicker than it is in adults. It gradually becomes thinner, the central part in the adult being thinner than the periphery.

The embryological origin of the different layers is important pathologically, since conjunctival affections frequently invade the corneal epithelium, scleral the substantia propria, and uveal the endothelium and its contiguous layers.

Blood-vessels in the cornea are limited normally to a narrow peripheral zone, ½—1 mm. wide at the sides, 1—1½ or at most 2 mm. wide above and below (Leber). Here they form a series of minute loops, and it is by exudation from these that the whole cornea is nourished.

The epithelium is stratified, consisting of several layers. The basal cells are cylindrical, and differ from those of the neighbouring conjunctiva in that their nuclei are farther from the basement membrane and do not stain more deeply than those of the other layers (Fuchs).

Moreover they do not contain pigment granules, such as often occur in the conjunctiva of the limbus, and there are no papillæ. The cells of the middle layer are typical prickle-cells, so that there are definite lymph-channels between them, such as do not exist in the conjunctiva. The superficial cells are flattened, with oval nuclei lying horizontally.

The substantia propria consists of alternating lamellæ of connective tissue, each made up of bundles of fine fibrillæ. There are about sixty lamellæ (Bowman), which run parallel to the surface, and cross at right angles in alternate layers. They intercommunicate frequently, so that they cannot be stripped apart cleanly. The bundles of fibrils are roundish in cross-section, and are bound together by ground-substance. By means of injection under very low pressure, a network of anastomosing stellate spaces between the lamellæ is obtained. These are *v. Recklinghausen's canals.* If mercury is used and the pressure is greater, tubular passages running at right angles to one another in the different layers are injected (*Bowman's corneal tubes*). This is seen even better by injecting air, and is due to forcible separation of the lamellæ; the tubes stop at the sclerotic, where the tissue becomes denser. According to Leber, there are no preformed spaces between the lamellæ, and the circulation of fluid is entirely by diffusion.

There are two kinds of cells present between the lamellæ. The corneal corpuscles (Virchow) or fixed corneal cells (Cohnheim) are simply more highly differentiated connective-tissue cells, differing only in being more regularly arranged than usual, owing to the very regular arrangement of the lamellæ. They are flat, stellate cells with long ramifying processes, which anastomose with those of the other cells. They lie between the lamellæ, and are surrounded by lymph-spaces, which also communicate along the processes with those of neighbouring cells. The nuclei are round or oval in the new-born, but polymorphic in the adult, with several nucleoli. The cytoplasm is clear, except near the nucleus, where it is granular.

There are always wandering cells between the lamellæ (v. Recklinghausen), though these are normally few in number. They are derived from the peripheral blood-vessels, and are like wandering cells elsewhere. They are small and of very variable shape, and when fresh are strongly refractile and amœboid.

Hamilton states that in the kitten and probably in other animals the lymph-spaces are lined by a distinct endothelium, each cell having an oval or round nucleus. Rollet says that this is only found in young animals. Hamilton denies the existence of the corneal corpuscles, which he considers are simply spaces filled with albuminous fluid, which causes precipitation of gold from gold chloride. The nucleus really belongs to an underlying bundle of fibrous tissue.

Bowman's membrane is shown embryologically to be part of the substantia propria, and therefore totally different from Descemet's membrane. It does not stain with elastic-tissue stains, so that the term "anterior elastic lamina" is a misnomer. It differs from the other lamellæ in having no corneal corpuscles, and by ordinary stains appears structureless. It consists, however, like them, of fine connective-tissue fibres.

Descemet's membrane is a homogeneous elastic lamina, the product

of secretion of the endothelial cells covering its posterior surface. It stains with Weigert's elastic-tissue stain, acid orceïn, etc. It is normally uniformly thick in the central parts, but increases slightly in thickness at the periphery. It increases in thickness with age.

It is extremely delicate at the tenth week of fœtal life, and still very delicate at the fourth month. Up to this time Bowman's membrane is not yet visible. At the sixth month Bowman's membrane is distinctly seen, and Descemet's membrane is considerably wider than at the fourth month (Treacher Collins). It is about 5—7 μ thick soon after birth; 6—8 μ in the middle, and 10—12 μ at the periphery, at 20—30 years of age; and 10 μ in the middle, and 15—20 μ at the periphery, in old people (H. Müller). E. v. Hippel's measurements in the new-born were 2—2·4 μ after formol hardening, 3·6 μ after Müller's fluid. De Vries obtained the following results:—New-born, 1·5—2 μ; 10 years to adult age, 5—5·5 μ; 59—77 years, 6·25—8·75 μ. The increase in thickness with age bears no relationship to the increase in thickness of the whole cornea. Faint lamellation of Descemet's membrane can sometimes be made out in the normal eye, and frequently under pathological conditions.

Descemet's membrane is covered posteriorly by a single layer of endothelial cells, which are continuous with those which cover the ligamentum pectinatum iridis and the iris. The cells are flattened polygonal cells with distinct nuclei. According to Smirnow, and Nuel and Cornil, the cells are fibrillar in structure, being traversed by radiating bundles of fine fibrils, which pass from cell to cell across the intracellular spaces. These are probably threads of protoplasm; they soon disappear after death or removal of the globe. They have only been found in birds.

The presence of elastic fibres in the substantia propria has been the subject of dispute. It has been denied by Sattler and Stutzer, and affirmed by Leber, Kiribuchi, Prokopenko, and Tartuferi. Kiribuchi found fine fibrils by the resorcin-fuchsin method, and this was confirmed by Prokopenko by the acid-orceïn method. They were demonstrated in great profusion by Tartuferi by a silver impregnation method.

The cornea is traversed by networks of nerve-fibrils, derived from a peripheral *annular plexus*, which is supplied by 40—45 nerves from the ciliary nerves (Waldeyer). The nerves retain their medullary sheaths for 1—2 mm. and then form a *fundamental plexus* near the anterior surface of the substantia propria. From this, pencils of fibrils pass towards the centre of the cornea, interlace, and form a *subepithelial plexus*, from which minute varicose fibrillæ pass between the epithelial cells almost to the surface. There are wider meshed networks in the deeper layers of the substantia propria. The fibrils are surrounded by lymph-sheaths, the endothelial cells of which lie in close relation to the corneal corpuscles. The nerves can be often seen passing through Bowman's membrane. They are beautifully displayed by gold chloride, Ehrlich's methylene-blue method, or the Golgi method (Bach).

In old age the cornea becomes thinner, the lamellæ being more closely packed and the corpuscles flatter, their nuclei staining less deeply. As a result of these changes the cornea is duller, and its refrac-

tive index is increased, so that it reflects oblique light more strongly. Other specific changes may also occur, *e. g.* the formation of arcus senilis (q. v.) and hyaline bodies upon Descemet's membrane (q. v.).

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WOUNDS

UNCOMPLICATED WOUNDS

Wounds of the cornea may be partial—involving only the superficial layers—or perforating. In uncomplicated wounds the process of healing is the same in each case.

The healing of simple wounds of the cornea, such as are made by a keratome or Graefe's knife, have been investigated upon animals, chiefly rabbits, by Güterbock, Gussenbauer, Wyss, Neese, Ranvier, Clarke, etc. The wound made by a keratome or broad needle is probably the simplest linear wound which can be made, and heals most rapidly, the loss of tissue and the disturbance of the structures being minimal. On withdrawing the instrument after making a perforating wound, the aqueous escapes. It is rapidly secreted again, but the new-formed aqueous differs from the normal in containing a larger amount of proteid.[1] It is now capable of forming a fibrinous coagulum, and this is of importance in the process of healing.

The wound is rapidly closed by the apposition of the edges. This takes place only in the middle or slightly posterior layers of the substantia propria, and is brought about by the imbibition of fluid by the corneal lamellæ, whereby they swell, so that the cut ends come in contact. The area of contact is greater in wounds which traverse the cornea obliquely, and the cohesion is thus increased, so that these wounds are somewhat valvular. The cohesion rapidly becomes sufficient to withstand the intra-ocular pressure, so that the anterior chamber is re-formed. The time which this takes varies according to the nature of the wound, commencing within two minutes (Clarke), and being complete within half an hour in favourable cases. It may be delayed to two or three hours if the animal is not kept at rest (Clarke), or even to days or weeks under unfavourable conditions. Under these circumstances the nutrition of the cornea is liable to suffer.

At the anterior and posterior surfaces the wound gapes, owing to the normal elasticity of the tissues, which retract, leaving anterior and posterior triangular areas, the apices of which are directed towards the coherent part. The anterior edges usually project considerably above the

[1] See PARSONS, The Ocular Circulation, London, 1903.

surface of the cornea, the resistance to swelling of the tissues being least here (Fig. 83). The swelling is also partly due to tears. The anterior triangle is quickly filled with epithelium (twenty-four hours). This is not due to epithelium being carried in by the knife (Güterbock), since no epithelium is present at first, but the edges are covered in from twelve to fifteen minutes. The process is probably at first simply mechanical (Ranvier). The epithelial cells are normally in a state of tension, and when this is released movement takes place in the direction of least resistance. This view is supported by the fact that mitotic figures are absent from the cells in the depression at this stage, and only occur here late and sparsely, though this may be accounted for to some extent by direct cell-division, which takes place in epithelium which is dividing rapidly. Karyokinesis occurs first a short distance around the wound, and later in still more peripheral parts (Neese). This doubtless increases the tension of the cells where it occurs, and tends to push the older cells

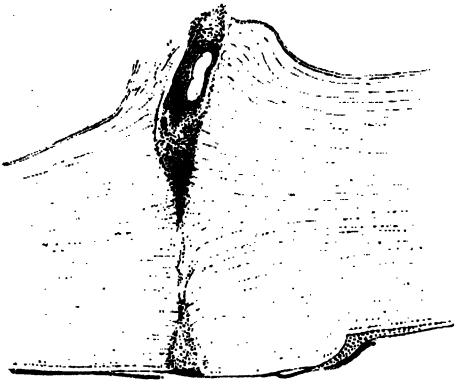


FIG. 83.—WOUND OF CORNEA.

Fuchs, T. O. S., xxii. Swelling of the lips of the wound through imbibition of fluid by the lamellæ.

into the wound. Still later, in about twelve hours, mitoses are found in the epithelium filling the wound itself. Peters described amœboid movements in the cells at the edges, but this observation has not been confirmed. The ingrowth of epithelium ends usually in about twenty-four hours, after which a process of consolidation sets in. The apex of the anterior triangle is often half or two-thirds of the way through the cornea.

Weinstein's results differ from those here described. He found mitoses—always in the cylindrical cells—as early as one hour after the operation. They occurred at a very considerable distance from the wound. In three hours mitoses were very numerous, and were found very near the wound, but not actually at the edge. In four hours they were found within the anterior triangle, as well as near the wound, and indeed over the whole surface of the cornea. At this stage cell-division is at its height. Direct cell-division (Nussbaum, Marchand) was not observed.

The posterior triangle is smaller, and similarly, though more slowly, filled with the endothelium (Schottländer, Peters). Descemet's membrane is more elastic, and therefore retracts more than any other part of the cornea. The cut ends curl up into a spiral, which is directed forwards, the anterior surface of the membrane retracting most. The endothelial cells are carried into the wound, and form heaps of cells at the edges. Small wounds are covered in three or four days, larger ones in seven days. There are no mitotic figures for six days, and they are not numerous until ten days and later; they are found chiefly near the periphery of the wound.

On the second day Weinstein found shapeless cell-masses on the convex surface of the ends of Descemet's membrane. No nuclei could be seen in them, but they stained deeply with hæmatoxylin. On the third day spindle-shaped cells were seen along the posterior surface of



FIG. 84.—WOUND OF CORNEA. × 55.

Healed iridectomy wound. The disturbance of parts is minimal. In the lower half there is extremely little scar tissue. The upper half contains more scar tissue, and is infiltrated with round-cells.

the wound. These gradually increased in numbers until they formed a long band, uniting the ends of Descemet's membrane. There were also some shorter, larger cells, with well-formed nuclei, often showing mitotic figures. They lay on the spindle-cells, projecting into the anterior chamber. All these cells are probably of endothelial origin.

Two processes therefore occur both in the epithelium and the endothelium: (1) a provisional covering of the wound with old cells; followed by (2) regeneration by karyokinesis, and ultimate consolidation (Peters).

The cut ends of Descemet's membrane never unite, but in the course of time a new cuticular membrane may be formed by the activity of the endothelial cells (Gepner, Wagenmann). In Wagenmann's case the new membrane was about one-fourth the thickness of Descemet's membrane in two and a quarter years.

It may ultimately become as thick as the normal membrane, and even fuse with it; but if the ends of the latter are curved forwards it fuses with the convex surface, so that Descemet's membrane appears to split. There are often several irregular cuticular membranes formed, each being generally covered by a layer of endothelium. Descemet's membrane then seems to split into several layers. They are usually thinner than the normal membrane.

O. Becker found the cut ends of Descemet's membrane still ununited in a scar after six years, and Neese experimentally confirmed the fact that they do not unite. Weinstein found the first signs of a new hyaline membrane four weeks after the operation. It was extremely thin even after two months, and was about half the thickness of the



FIG. 85.—WOUND OF CORNEA. × 55.

Wound with a fragment of steel, which was removed by Haab's magnet. Wound depressed; iris adherent. Bowman's membrane is curled up. The scar tissue binds the lamellæ together, and sends short conical processes between them. The retracted cut ends of Descemet's membrane are well seen. The inflamed iris stroma is seen below.

normal Descemet's membrane after three to three and a half months. In four months it nearly reached the normal thickness. The new membrane sprang from the convex surfaces of the cut ends of Descemet's membrane, but was continuous with the ends in rare cases in which these were very little bent forwards. Both membranes stained equally with Weigert's resorcin-fuchsin stain. The anterior half of the new membrane often showed fine striation longitudinally. Weinstein combats the theory of Ranvier, Wagenmann, etc., that Descemet's and the new membrane are the product of the endothelial cells. He regards them as differentiated corneal lamellæ which have

undergone hyaline changes under the influence of the aqueous fluid. The impermeability of the normal endothelium to the aqueous would seem to negative this view.

The substantia propria never regenerates; it is replaced by scar tissue. The ends of Bowman's membrane are slightly retracted, or may ultimately override one another, or be convoluted, through the contraction of the scar tissue (Fig. 85). The lamellæ are not always in contact even in the middle; they are then separated by a fibrinous coagulum containing very few leucocytes. Apart from œdematous swelling of the ends of the lamellæ and the neighbouring corneal corpuscles, there are no changes in the early stages. Later, the corneal cells proliferate into the clot and into the epithelium, which they push upwards towards the surface. The new cells are small and spindle-shaped, in no way differing from the embryonic connective-tissue cells of granulation tissue. From these, fibrous tissue fibrillæ are formed, running in irregular bundles—horizontal, oblique, and vertical. As time goes on the bundles become more horizontal, conforming to the general direction of the corneal lamellæ, the cells diminish in number, and a compact scar is formed (Figs. 84, 85). This dwindles more and more by the contraction of the scar tissue, but never entirely disappears. The younger the cornea, the more does the scar approximate to the structure of the normal tissue. Finally, the epithelium is lifted up almost or quite to its normal level, and only a linear cicatrix remains (Fig. 85).

Weinstein found that the fibrinous coagulum filling the wound played no active part in the healing process, but formed merely a temporary plug, and a framework for the wandering cells and histogenetic elements. After three or four hours' deeply staining, spindle-cells with very dark thin linear nuclei are seen in the substantia propria near the wound. These often form chains, two, three, or four in a row. The author is doubtful as to their origin, and quotes Ballowitz, who never observed mitosis in the normal corneal corpuscles. They are most probably leucocytes, which Weinstein states were entirely absent. He observed mitoses in the fixed corpuscles, but not until the second day. They occurred in spindle- and club-shaped cells close to the wound, and increased in numbers, so that by the fifth or sixth day the wound was filled with young spindle-cells. The process goes on with varying rapidity in different wounds, and in different parts of the same wound.

Weinstein describes vacuolation and degeneration of the epithelial cells of the anterior triangle as regeneration of the substantia propria proceeds. Many nuclei shrink, and the cells break down, forming round or oval spaces. Groups of epithelial cells may become entangled in the granulation tissue. These processes obviously assist the restoration of the normal disposition of the parts.

Masugi has also investigated the subject, especially from the point of view of the effect of cocain on the regenerative processes. He confirms most of the results of earlier observers, and finds further that cocain has a deleterious effect upon the cells, diminishing karyokinesis.

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Virchow's Archiv, lxix, 1877. NEESE.—A. f. O., xxxiii, 1, 1887. PETERS.—Inaug. Diss., Bonn, 1885. RANVIER.—Comptes rendus, 1896, 1897, 1898; Arch. d'Anat. micr., 1898. SCHOTTLÄNDER.—Arch. f. mikr. Anat., xxxi. PETERS.—Arch. f. mikr. Anat., xxxiii. GEPNER. —A. f. O., xxxvi, 4, 1890. WAGENMANN.—A. f. O., xxxvii, 2, 1891. CLARKE.—T. O. S., xviii, 1898. MASUGI.—K. M. f. A., xxxix, 1901. FUCHS.—T. O. S., xxii, 1902. *WEINSTEIN.—A. f. A., xlviii, 1903.

COMPLICATED WOUNDS

Wounds of the cornea are often accompanied by *striate opacities* (q. v.), and less commonly by so-called *filamentary keratitis* (q. v.).

The most frequent complication is the intrusion of some foreign body between the lips of the wound. This is usually either the iris, lens fibres or capsule, or the vitreous; rarely cilia, etc., or the detached retina.

The iris.—When a perforating wound or ulcer lies in front of the iris, the latter is liable to be carried into the wound by the sudden outward rush of aqueous (Fig. 86). The prolapse of iris may be partial or complete, a knuckle of iris protruding for a variable distance into the posterior part of the wound, or the iris hanging free with the pupillary border outside the wound. If the iris is for some time in contact with the wound, adhesion takes place, and an *anterior synechia* is formed. The adhesion is at first by means of exudate; later, as the process of cicatrisation proceeds, the iris becomes anchored to the cornea by new-formed fibrous tissue. In course of time the iris stroma atrophies at the point of attachment, and is replaced by scar tissue, the retinal epithelium alone persisting for a long period.

The anterior synechia of the iris need not necessarily be exactly at the site of the wound, but is always in its immediate vicinity. The endothelium of Descemet's membrane is then absent at the site of adhesion, and is replaced by layers of long spindle-shaped cells with rod-shaped nuclei; these cells are modified endothelial cells. They often fill the angles between the iris and Descemet's membrane. The endothelium covering the anterior surface of the iris is liable to form a hyaline cuticular membrane upon its surface when subjected to the chronic irritation induced by the synechia, so that in old synechiæ Descemet's membrane may appear to pass on to the surface of the iris, or to split at the edge of the adhesion, one part being the true membrane, the other the new-formed one (Fig. 89).

Other structures besides the iris may adhere to the back of the cornea after perforating wounds, such as the lens (Fig. 94), vitreous (Fig. 88), or retina. Such cases are rarer, and are usually accompanied by anterior synechia of the iris; indeed, there is generally an anterior staphyloma. In the case of the lens there is usually a traumatic cataract; the capsule is ruptured and lies convoluted in or near the wound (Figs. 86, 91, 92). The lens is usually cataractous throughout, and is invaded by fibroblasts at the site of injury. These subsequently form scar tissue, and tie down the lens firmly to the cornea.

Adhesion of the vitreous can only occur after dislocation or removal of the lens (Fig. 88). The vitreous becomes invaded with young connective-tissue cells from the cornea, and these radiate from the



FIG. 86.—WOUND OF CORNEA. × 28.

Peripheral wound, with prolapse of iris. The central lip, which is covered by epithelium, overrides the peripheral, to which the iris is adherent. The lens capsule is prolapsed into the wound. Below on the right the ciliary processes are seen.

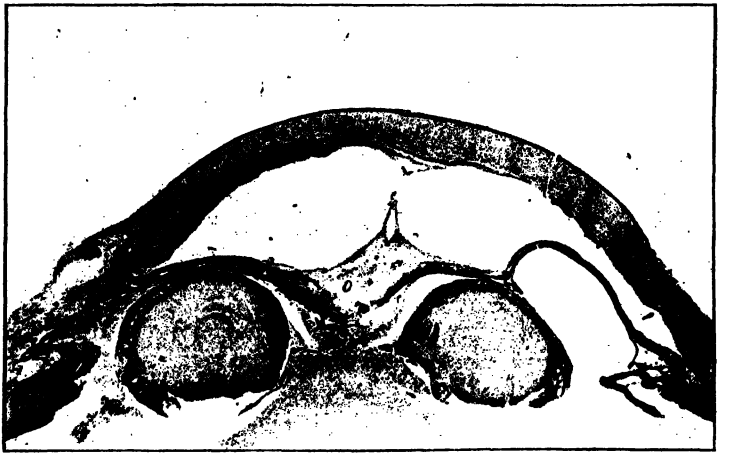


FIG. 87.—WOUND OF CORNEA. × 8.

Wound in centre of cornea sixteen years ago. Corneal scar, with thinning of epithelium, showing "levelling tendency." Absorption of centre of lens, and bombé iris. The pupil is occluded with vascular fibrous tissue, which stretches forwards to the back of the cornea. Here the endothelium has proliferated, and grown down over the fibrous tissue, subsequently producing a hyaline membrane. The dark spots in the lens are due to calcification.

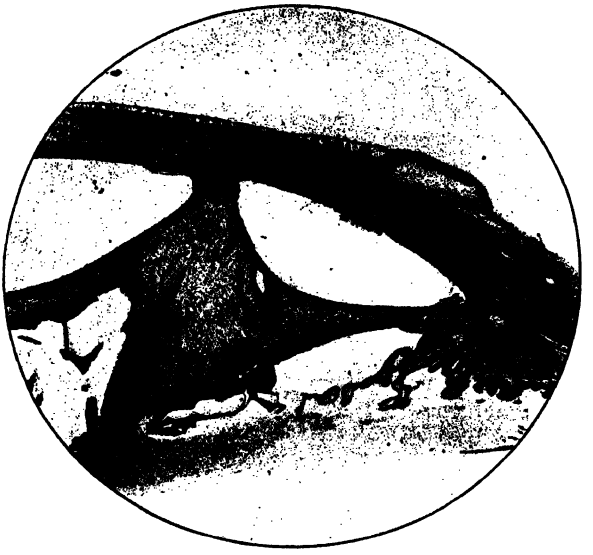


FIG. 88.—WOUND OF CORNEA. × 10·5.

Old perforating wound. The figure, which does not pass through the actual wound, shows anterior synechia of iris and vitreous. The mass consists of loose fibrous tissue containing iris stroma, with many branched chromatophores. Note œdema of corneal epithelium.



FIG. 89.—WOUND OF CORNEA. × 20.

Wound of cornea with inclusion of a knuckle of iris; the scar has stretched, producing the appearance of a ciliary staphyloma. Note the "ectropion of uvea" and folding of the cut Descemet's membrane, which appears to split at the false angle, a new delicate hyaline membrane passing over the iris from it to the edge of the out-turned retinal pigment. Descemet's and the new membrane have a single layer of endothelium.

adhesion, being most numerous at this site. The microscopical structure of the vitreous under these conditions very nearly resembles that of cyclitic membranes, bands of fibrous tissue radiating backwards, gradually becoming more and more attenuated. They consist chiefly of long spindle-shaped cells with elongated oval nuclei, lying amidst extremely delicate fibrillæ. In these cases also the endothelium of Descemet's membrane often grows on to the new tissue, and subsequently forms a hyaline membrane. Endothelial cells are also found scattered amongst the fibres.

In a *partial prolapse of iris*, a knuckle of iris projects into the wound, and may appear upon the surface as a grey or brown prominence (Fig. 89). The anterior surface of the iris becomes fused with the



FIG. 90.—CYSTOID CICATRIX. × 17.

Six months after iridectomy for glaucoma. The projecting lower lip consists of corneal lamellæ, little changed, covered on both sides by the iris, only slightly atrophic. The bay consists of conjunctiva, lined by much atrophied iris, little but the retinal epithelium persisting. The iris is adherent to the anterior lip, but not to the cornea anterior to this.

edges of the wound exactly as in the case of a simple anterior synechia. Any portion which projects above the surface of the cornea becomes covered with a layer of exudate, over which the epithelium grows with extreme rapidity, so that it is usually covered in about twenty-four hours. The exudate is replaced by granulation tissue, which at first forms grey stripes. The contraction of the new-formed fibrous tissue tends to flatten the prominence, and a firm grey scar may result. In other cases the scar tissue is not strong enough to withstand the intra-ocular pressure, and a *cystoid cicatrix* is formed (Fig. 90), the wall consisting of epithelium, a thin layer of scar tissue, and the retinal pigment layer of the iris. The scar tissue is often so thin that the cicatrix looks black.

If the iris fills only the posterior part of the wound, the anterior part may cicatrise in the usual manner, most of the cells being directed vertically, their union with the iris being looser than with the corneal lamellæ. In this case also cystoid spaces may be formed, but they are now situated anterior to the iris, and have the retinal pigment upon their posterior surface, thus differing from the cystoid cicatrix, which is merely an outlying bay of the anterior chamber, covered anteriorly by the retinal pigment.

In *complete prolapse of the iris*, and in extensive partial prolapse, the pigment epithelium also breaks down, the pigment granules are taken up by leucocytes and also float free in the lymph-spaces. Some are



FIG. 91.—PERFORATING WOUND OF CORNEA. × 25.

Five weeks after removal of chip of steel by Haab's magnet. Cornea retracted at wound. Bowman's membrane folded; triangular space in back of cornea filled in with new fibrous tissue, which also anchors up the lens capsule, and thus pulls forward the iris. The lens capsule seen in the figure is filled with red corpuscles; below and to the left of it are lens fibres.

carried into the epithelium, where they lie both between and in the cells. Other masses of pigment become permanently embedded in the scar, and apparently undergo little change after many years.

Fragments of iris may heal into the wound with but little inflammatory reaction (*cf.* lens capsule, p. 161). Wounds with anterior synechiæ or prolapsed iris are, however, a constant source of danger. Every movement of the iris drags upon the ciliary body, owing to the firm anterior attachment, and this may lead to ciliary irritation. Moreover the consolidation of the scar is interfered with, so that a weak spot is left, which is vulnerable to both mechanical and bacterial agencies.

The lens and vitreous.—Lens fibres (Fig. 92) and vitreous intruded

between the lips of the wound delay union, and are a source of danger, since they form a track along which infection from the conjunctival sac may travel. They are partly cast off into the sac and partly absorbed. The granulation tissue invades them, and eventually they are replaced by scar tissue (Fig. 91).

The lens capsule is much more dangerous (Fig. 92). It is always convoluted, and appears to be of irregular thickness in sections, owing to the different directions in which it is cut. It is always surrounded by marked lymphocytic infiltration, showing severe inflammatory reaction. This is liable, in the course of time, to attack the deeper parts of the eye, leading especially to cyclitis. It occurs in the absence of bacterial infection, inoculation and culture showing the eye



FIG. 92.—WOUND OF CORNEA. × 25.

Iridectomy for acute glaucoma; lens wounded; no iridectomy effected; prolapse of lens and vitreous; large subchoroidal hæmorrhage. The wound is filled with folded capsule containing swollen lens fibres. The iris lies against the cornea below, and behind this are ciliary processes, pushed forwards, folded lens capsule, and detached choroid containing blood. To the right of the wound are iris pigment and extravasated blood.

to be sterile. The irritation is probably due to the extreme resistance of the capsule to absorption, whereby the healing of the wound is delayed, and satisfactory consolidation is indefinitely postponed. The granulation tissue around the capsule is often œdematous, and frequently contains cystic spaces. A more acute inflammation is not infrequently set up by bacterial infection along the spongy track, and the eye is lost by panophthalmitis.

The ciliary body.—When the wound is very peripheral, as in some iridectomies for glaucoma, etc., the ciliary processes may prolapse through the wound (Fig. 93). These can scarcely be called corneal

wounds, as they occur in the sclera just posterior to the corneo-scleral margin. They behave, however, in much the same way as corneal wounds. The prolapsed ciliary processes become adherent to the posterior lip of the wound, and usually retard healing. Moreover, the ciliary body is thus exposed to grave danger from infection, and the complication must be regarded as one of the most serious which can attend an iridectomy. Such eyes usually demand excision on account of the dangers of sympathetic ophthalmia,—and that before consolidation of the scar has had time to occur. Hence we usually see little evidence of the process of repair, intense inflammatory reaction being the most noticeable feature.

Cilia, etc.—Cilia and other foreign bodies may be carried into the wound; they may rarely be inert, inducing no marked inflammatory reaction. Cases of cilia in the cornea have been described by Alt, Schwarz, and others. Most frequently they set up inflammatory reaction, the irritation being shown by the development of giant-cells, usually

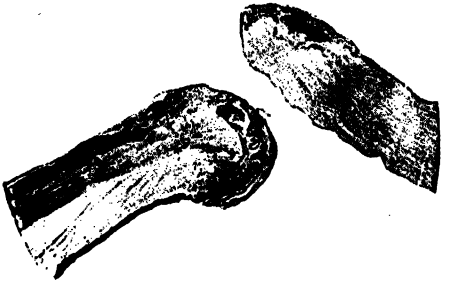


FIG. 93.—PROLAPSE OF CILIARY BODY.

From Treacher Collins, Researches. Glaucoma of two months' standing; section very peripheral. Prolapse of ciliary body; escape of lens the day after operation.

typical myeloplaques (Schwarz). If the root-sheath is present, the epithelial cells proliferate, forming pearl tumours or cysts (*v. infra*).

ALT.—Lectures on the Human Eye, New York, 1880. SCHWARZ.—A. f. O., xlvii, 1898.

The retina. — In operations upon glaucomatous eyes the retina may become detached and may prolapse into the wound. Such eyes are usually excised before the wound has had time to heal. After expulsion of the lens the retina may become adherent to the back of the corneal scar.

If a perforating wound is opposite the pupil, it cannot be covered by iris. In such cases adhesion of the lens may occur (Fig. 94). More commonly the wound heals slowly by outgrowth of cicatricial tissue from the margins of the opening. Sometimes the plug of exudate or the delicate granulation tissue blocking the wound is displaced, either by the rising intra-ocular tension, or generally by improper behaviour of the patient. This may occur repeatedly, and ultimately the perforation may remain permanently open, and a *corneal fistula* is formed. According to Czermak, the formation of a fistula is

aided by adhesion of the pupillary border of the iris to the edge of the wound. Every dilator action then pulls upon the granulation tissue, which is unable to consolidate. It becomes loose and spongy, filled with cystic spaces, and covered only by epithelium, which is also

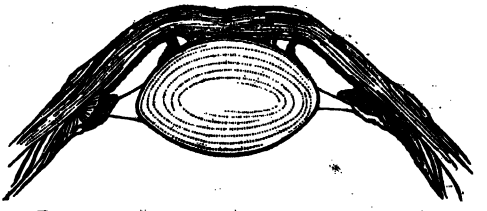


FIG. 94.—PERFORATION OF THE CORNEA.
From Lawson, after Priestley Smith. The iris is adherent to the cornea, and there is a ring posterior synechia; the lens is adherent to the pseudo-cornea.

vacuolated and œdematous. There is grave danger in these cases of the epithelium growing down along the sides of the wound into the anterior chamber or on to the iris. Such growth will definitely prevent cicatrisation of the wound, and the fistula will be permanent

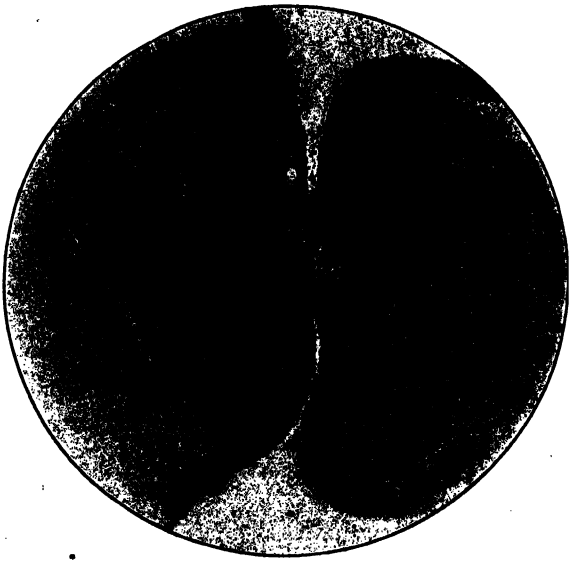


FIG. 95.—WOUND OF CORNEA. × 60.
Perforating corneo-scleral wound six days after injury. One edge overrides the other, the interposition of epithelium having prevented union. The epithelium and lamellæ are œdematous, the latter being swollen, so that their contours are indistinct.

unless it is removed. It has never been observed pathologically, except when the iris has been adherent.

CZERMAK.—A. f. O., xxxvi, 2, 1890; xxxvii, 2, 1891.

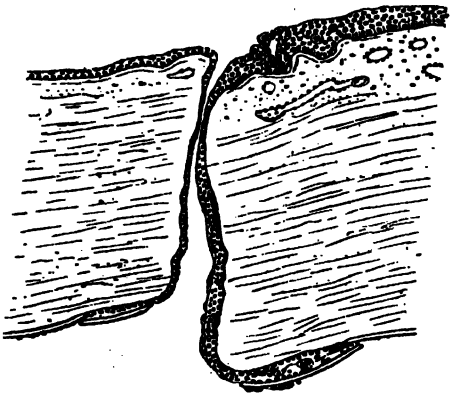


FIG. 96.—WOUND OF CORNEA.

Fuchs, T. O. S., xxii; *see also* Meller, A. f. O., lii. Four days after cataract extraction. Downgrowth of epithelium over edges of wound and between Descemet's membrane and the substantia propria.



FIG. 97.—EPITHELIUM IN ANTERIOR CHAMBER. 28.

From a man æt. 70. November 4th, 1899, preliminary iridectomy; January 24th, 1900, extraction; January 12th, 1901, needling; July 23rd, 1902, excision. The eye was regarded as dangerous and likely to set up sympathetic inflammation, though there was no k. p. in the other eye. It is interesting to note that there are nodular aggregations of lymphocytes in the iris and ciliary body. There is an anterior synechia, densely infiltrated with lymphocytes; it is invaginated by a fold of epithelium, which extends along the back of Descemet's membrane. Note the new hyaline membrane, covered with endothelium, on the *inner* surface of the epithelium; the appearance of splitting of Descemet's membrane is seen at the extreme anterior part of the figure.

In some cases of wound of the cornea or limbus, *e. g.* cataract extraction or iridectomy, the edges do not lie in complete apposition (Fig. 95). The normal pushing inwards and subsequent proliferation of epithelium is then liable to be more extensive (Fig. 96). The epithelium grows in over both edges of the wound, and may pass down into the anterior chamber, and even cover the back of the cornea and pass on to the iris (Fig. 97), finally lining the chamber completely (Fig. 98). The process is extremely rapid: Meller quotes a case in which both sides of an extraction wound were covered in four days. On reaching the back of the cornea the epithelium insinuates itself between Descemet's membrane and the substantia propria, and also grows on to the posterior surface. A variable number of layers of cells is formed, the lowest cells being cylindrical or cubical, the highest very

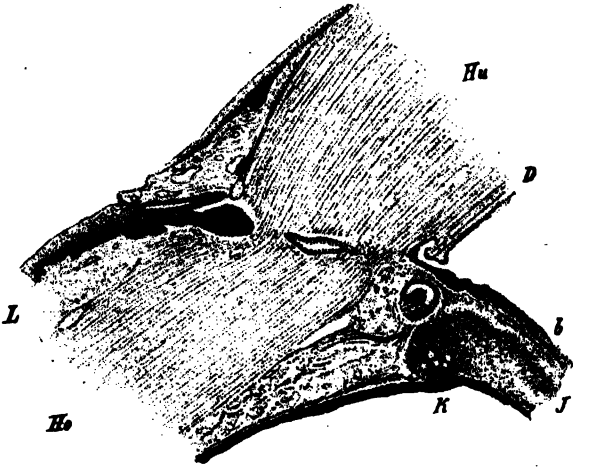


FIG. 98.—EPITHELIUM LINING ANTERIOR CHAMBER.

Fuchs, T. O. S., xxii; *see also* Meller, A. f. O., lii. Several years after cataract extraction. Downgrowth of epithelium into the anterior chamber, covering iris, Descemet's membrane, etc. There is a small epithelial cyst in the iris; this is merely the blind end of the epithelial invagination. *L*, limbus; *Ho*, corneo-scleral junction; *Hu*, cornea below wound; *D*. Descemet's membrane; *J*, iris; *K*, retinal pigment epithelium; *b*, epithelium on iris.

flat and long. The same applies when the iris is covered or the whole chamber lined; the epithelium varies extremely in thickness, from a single layer to five or six or more, and the cells are often ill-formed; sometimes they can be distinguished from endothelial cells only with difficulty.

Often these wounds heal normally in places, whilst in other places the epithelium grows in. The eye may therefore not require excision for a prolonged period. In such cases the downgrowths are extremely irregular and tortuous, so that the canal is cut across in various directions in sections. Appearances of solid downgrowths, of tubes, and of large cystic spaces are thus brought about. Such cystic spaces can only be distinguished from true implantation cysts by means of

serial sections. The wound edges, when clad with epithelium, cannot unite until this is destroyed. Doubtless this takes place to a large extent in the older cases, and the fistulous track which ultimately persists is so tortuous that the aqueous does not escape, or only in small quantities, the walls being pressed together by the agency of the intra-ocular pressure. The condition is quite likely one of the causes of a subsequent secondary glaucoma, normal filtration being prevented by the epithelial coat; in other cases the track probably acts like a filtering scar.

In one of Meller's cases the epithelium on the iris, etc., was a typical stratified epithelium, many of the cells being goblet-cells which discharged their contents into the anterior chamber. The epithelium here was probably derived from the conjunctiva.

The condition here described was first reported by Guaita, who regarded the epithelium as endothelium, and missed the true meaning of the phenomenon. It must have been observed by many others, and I have seen it several times, but Meller, working under Fuchs, was the first to give a comprehensive account.

GUAITA.—A. d'O., xiii, 1893. MELLER.—A. f. O., lii, 3, 1901.

ABRASIONS

Abrasions which involve only the epithelium are rapidly filled in, probably at first by the pressure of the neighbouring cells, and later by karyokinesis. Such abrasions heal without leaving any opacity.

When the injury extends deeper and involves Bowman's membrane,

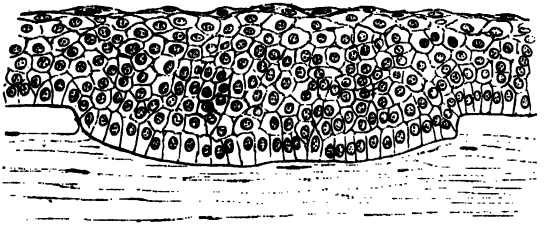


FIG. 99.—ABRASION OF THE CORNEA.

Fuchs, T. O. S., xxii. Facet, with destruction of Bowman's membrane, caused by a small corneal ulcer, filled in with epithelium. There was no opacity or alteration in level of the surface.

the loss of tissue is replaced in the same manner by epithelium (Fig. 99). Bowman's membrane is never re-formed, and the thickening of the epithelium persists for a prolonged period. In late stages it resembles the normal corneal epithelium, the basal cells being cylindrical and lying directly upon the substantia propria or upon a thin layer of scar tissue, the only difference being an increase in the number of the intermediate layers of prickle-cells.

Even when the loss of substance is greater and involves the superficial lamellæ, the wound is at first clothed with epithelium and then

filled in with the same cells. Karyokinesis then occurs in a zone around the wound, exactly as in the case of perforating wounds. The epithelium invades every crevice which is available, forming downgrowths and oblique or lateral processes into any artificial clefts and also into the interlamellar lymph-spaces (*cf.* Fig. 131). These processes are opposed by the proliferation of the corneal corpuscles, which gradually increases, especially after vascularisation of the superficial layers by vessels which grow in from the periphery and bring pabulum for purposes of regeneration. Ultimately the granulation tissue increases more rapidly than the epithelium, which is pushed more and more towards the surface. The larger downgrowths, however, often persist indefinitely. The granulation tissue is doubtless partly derived

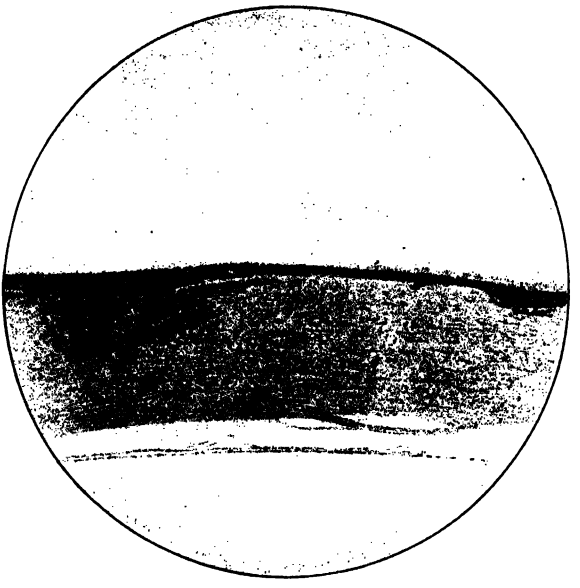


FIG. 100.—CORNEAL NEBULÆ. × 55.

Note the gaps in Bowman's membrane, filled in with epithelium lying upon scar tissue, which is vascularised in the larger deposit to the left.

from the walls of the larger new vessels, which possess a connective-tissue adventitia, the smaller ones being mere endothelial tubules. It is seldom very profuse, owing to the absence of vessels from the normal tissue. Finally the granulation tissue consolidates into scar tissue in the usual manner, the cells becoming spindle-shaped, and dwindling *pari passu* with the development of fibrous tissue. The bundles of fibres are smaller than the normal lamellæ and are disposed irregularly, so that a permanent *nebula* or *leucoma* results (Fig. 100). The leucocytes which were present in the granulation tissue disappear for the most part, but groups of lymphocytes often persist for a very long period. Most of the vessels also disappear, their walls falling together and forming part of the scar. Some of the larger vessels often persist, and continue

to carry blood. The epithelium may be even thinner than normal over the scar, but more frequently it remains thick, with an uneven basal line, so that irregular papillæ are formed. The larger down-growths generally remain, and are often club-shaped, being connected with the surface epithelium by a narrow neck. The epithelium may become epidermoid by cornification of the superficial cells, but this is seldom the case except in extensive injuries, and is most common in anterior staphylomata (q. v.).

ANTERIOR STAPHYLOMA

Anterior staphyloma is a protuberant cicatrix arising from a prolapse of the iris; it may therefore be *partial* or *total* (Fig. 101). It may follow a perforating wound, but is usually due to the perforation of an ulcer, especially such as is caused by ophthalmia neonatorum. The *primary protrusion* occurs at the moment of prolapse of the iris. Cicatrisation follows, and in the case of small prolapse may lead to flattening of the scar. In other cases of small, and in all cases of large prolapse the contraction of the scar tissue is insufficient to bring this about, and the soft cicatrix yields to the normal intra-ocular tension. Generally the prolapse of the iris leads to blocking of the angle of the anterior chamber, the intra-ocular tension rises, and the cicatrix yields still more, or, if it was previously flat, *secondary protrusion* may take place.

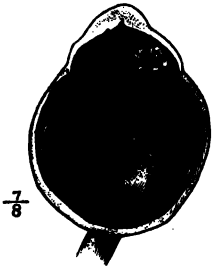


FIG. 101.—ANTERIOR STAPHYLOMA.

After Lawson. From the R. L. O. H. Museum.

Partial staphylomata are usually conical, rarely hemispherical; they usually extend to the margin on one side. Total staphylomata, on the other hand, are usually hemispherical, rarely conical; there is invariably a rim of cornea around the pseudo-cornea, even in the worst cases, this rim being well nourished by the peripheral blood-vessels and never necrosing through ulceration. Spherical staphyloma is due to an extensive perforation; the cornea in the vicinity of the opening is of normal thickness, and the prolapsed iris projects at right angles. In partial staphyloma the perforation is less extensive and the cornea tapers down towards the opening, but at the same time affords considerable support to the iris (*cf.* Fig. 104).

The thickness of a staphyloma varies very greatly in different cases, and often in different parts of the same case. In the latter, bands of cicatricial tissue develop, whilst the intermediate parts are less supported and project more; in this manner a *racemose staphyloma* is produced.

In the earliest stage there is merely a prolapsed iris covered with exudate, which also fills the pupil. The iris is acutely inflamed and densely infiltrated with leucocytes. Granulation tissue forms upon this surface, often in large masses, which may contain iris pigment, etc., and remnants of the lens capsule and lens, if this has been expelled from the eye (Fig. 103). Epithelium grows over this granulating surface,

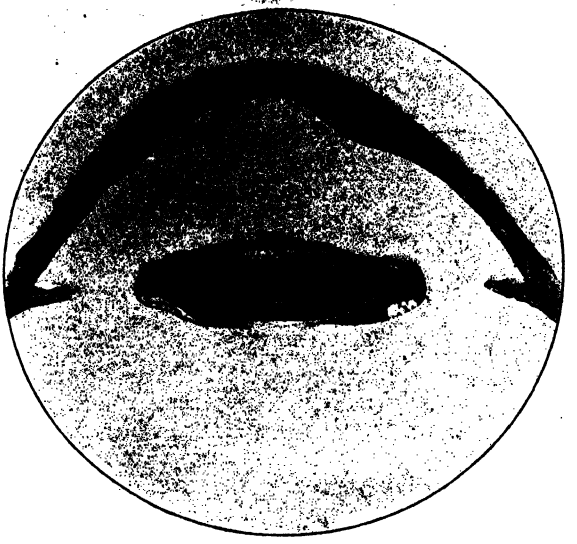


FIG. 102.—ANTERIOR STAPHYLOMA AND ANTERIOR CAPSULAR CATARACT. × 5.

From a boy æt. 2; the result of ophthalmia neonatorum. The staphyloma is partial, limited to the lower part (on the left of figure). Here the epithelium is epidermoid and horny, the cornea is replaced by fibrous tissue, and the iris is reduced to a layer of pigment epithelium. On the right Bowman's membrane is destroyed, the substantia propria is infiltrated in the anterior layers, the posterior being intact, and the iris is only slightly degenerated. The ciliary body is atrophic, the processes being stretched inwards. The lens shows a well-marked anterior capsular cataract.

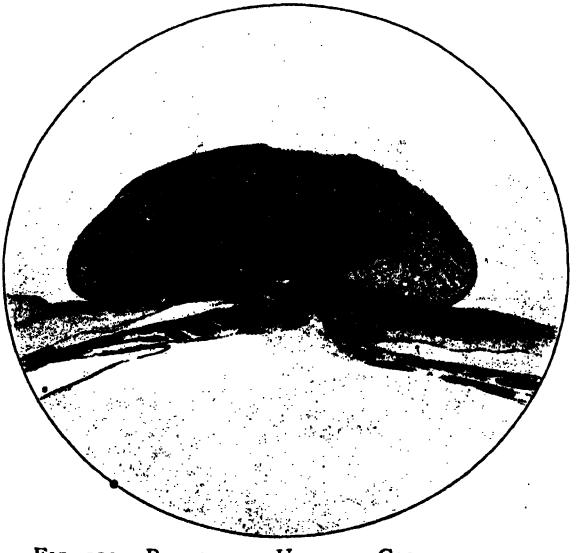


FIG. 103.—PERFORATED ULCER OF CORNEA. × 9.

From a child æt. 3 weeks; ophthalmia neonatorum. The cornea has perforated, the lens has been expelled, and the iris has prolapsed. A large mass of granulation tissue, partly covered by epithelium, has formed upon the ulcer. The lighter area in this, to the right, is occupied by a fragment of convoluted lens capsule.

filling the crevices and developing at first irregularly, as in all such conditions. The granulation tissue gradually develops into scar tissue in the usual manner, which need not be recapitulated. The iris stroma is only apparent in the early stages; it slowly atrophies, and usually becomes entirely replaced by fibrous tissue. The uveal pigment persists, at first as a well-defined layer. Later it becomes broken up; cells or clumps of pigment or isolated granules are found scattered in the scar, but the main part lines the staphyloma. As this stretches the pigment layer atrophies in parts, and the remainder becomes transformed into a network, which varies greatly in different cases.

The thickness of the staphyloma depends chiefly on the amount of scar tissue, though the epithelium also differs in this respect. It may be as thin as paper, and is not often thicker than the normal cornea. The epithelium may grow directly on the prolapsed iris, the granula-

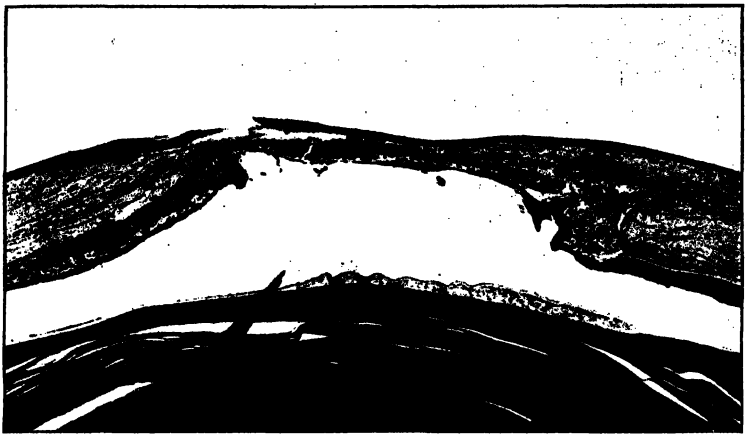


FIG. 104.—ADHERENT LEUCOMA. × 25.

From a man æt. 61; following perforating ulcer. The central part consists of degenerated iris, containing the sphincter, covered by epithelium; the thicker part to the right of the centre has a few corneal lamellæ interposed. At the extreme right and left the cornea is of average thickness, but is infiltrated and vascularised anteriorly. There is an anterior capsular cataract.

tion tissue being reduced to a minimum (Fig. 104). Often Descemet's membrane is prolapsed and convoluted (Fig. 105), and I have seen the epithelium growing upon this, filling in all the convolutions.

The epithelium is usually very thick, often showing downgrowths or forming true papillæ. There are sometimes epithelial nests, and prickle-cells are generally developed in the middle layers. It frequently becomes typically epidermoid; keratohyalin granules form in the upper layers, staining deeply with hæmatoxylin or by Gram's method, whilst the surface layers lose their nuclei and become horny (Fig. 106). Various degenerative changes occur in the epithelium, especially over calcareous deposits (Fuchs) (*v. infra*), and atheromatous ulcers occur in these eyes (q. v.). Spaces form in the epithelium, separated by thin walls of



FIG. 105.—ANTERIOR STAPHYLOMA. × 60.

From a specimen by Verhoeff. This resembles the edge of the bay in Fig. 104. On the right is the cornea, around the edge of which the ruptured Descemet's membrane is much folded. Below this the iris is of normal thickness; anteriorly it is spread out over the edge of the cornea, and more to the left it is thin and covered directly by epithelium.

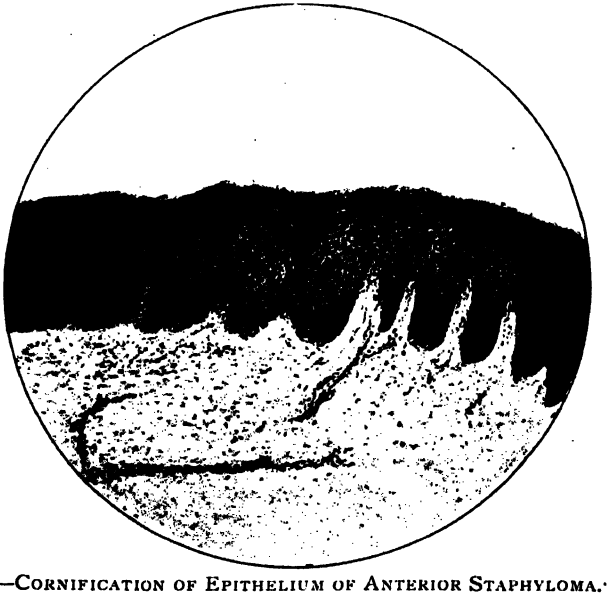


FIG. 106.—CORNIFICATION OF EPITHELIUM OF ANTERIOR STAPHYLOMA. × 55.

From an anterior staphyloma of twelve years' duration. The epithelium is typically epidermoid, with well-marked true papillæ. The superficial cells are corneous, devoid of nuclei; the layer below this contains granules of keratohyalin. Note the blood-vessels in the pseudo-cornea.

shrunken cells; they are formed between the cells and not by vacuolation, and are often covered by a single layer of epithelium only.

The scar tissue consists of very dense fibrous tissue, with few cells and few vessels. Pigment is found here and there, and calcareous deposits often occur. Sometimes the fibrous tissue shows hyaline degeneration, and masses of hyaline or granular material may replace the superficial layers. The hyaline deposits may occur as granules, globules and concretions, or great masses and whorls of hyaline fibrous tissue may be found (*v. infra*, "Degenerations"). The thickness varies much in different parts, owing to the bands which project upon the posterior surface. At the extreme periphery remnants of Bowman's and Descemet's membranes may be found.

Sachsalber found large numbers of elastic-tissue fibres in the sclera,

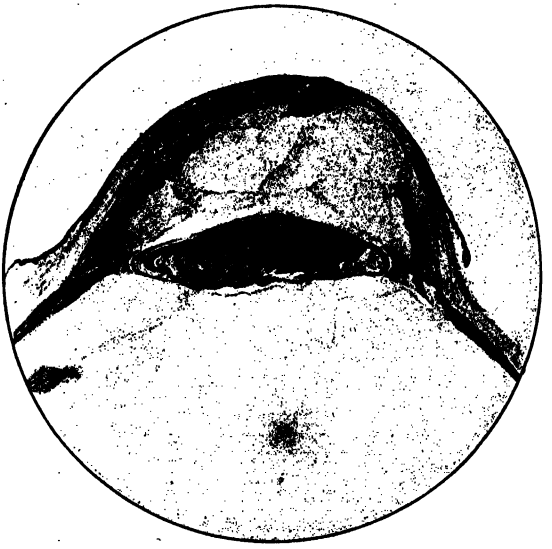


FIG. 107.—ANTERIOR STAPHYLOMA.

Photograph by Lister. From a child æt. 2 years 8 months. There is an area of purulent infiltration, stained dark in the figure. The posterior chamber is full of fibrin and leucocytes.

episclera, peripheral part of the cornea, and to a less extent in the conjunctiva in cases of anterior staphyloma. These form fine, very wavy fibres, which stain deeply with eosin; they increase in length and breadth, become spiral and irregular in thickness, and finally break up into hyaline granules and clumps. The condition is allied to that found in pinguecula.

In some of the hyaline deposits in anterior staphyloma Beselin obtained a typical amyloid reaction with iodine and iodine violet, whereas with gentian violet and methyl violet the reaction was inconclusive. There is therefore the same uncertainty about the chemical nature of the deposits in this situation as in the conjunctiva and elsewhere (*v.* p. 96).

Schiele, using the iodine test, found glycogen present in the epithelium, in newly formed connective tissue, and in the corneal corpuscles.

The anterior chamber is obliterated, whilst the posterior chamber is enormously enlarged. The ciliary body is usually atrophic, owing to the rise of tension, and the ciliary processes are dragged inwards and elongated by the fibres of the zonule of Zinn. The lens is often absent, having been expelled when the perforation occurred. In other cases it is cataractous and shrunken; frequently it shows an anterior capsular or a pyramidal cataract. It is often subluxated. The other parts of the eye show changes dependent chiefly upon the secondary glaucoma.

The fluid contained in the posterior chamber differs from normal aqueous. It is generally yellow, rich in proteids, and capable of coagulating. It often contains cholesterin crystals, blood, etc.

SACHSALBER.—B. z. A., xlviii, 1901. BESELIN.—A. f. A., xvi, 1886. SCHIELE.—A. f. A., xix, 1889.



FIG. 108.—KERATECTASIA. × 23.

From a man æt. 45; iridectomy at age of twelve. A. c. very deep; angles blocked. Cornea thickened in centre by hyaline degeneration (*v. infra*). Stretching of the cornea has produced rupture of Descemet's membrane, which is coiled forwards in a spiral at the inner end. A new hyaline membrane has been formed on the back of the cornea. These membranes show definite lamellation in places.

KERATECTASIA

Keratectasia is a protrusion of the cornea which sometimes follows inflammatory processes in it without perforation. It consists of corneal tissue, and the iris plays no part in its formation.

The cornea is softened by the inflammation or partially destroyed

by ulceration, so that it is unable any longer to withstand the normal intra-ocular pressure. If only Descemet's membrane persists, a *keratocele* is produced, and this may cicatrise in the form of keratectasia. It then forms a transparent vesicle projecting above the surface and surrounded by a ring of opaque cicatricial tissue. After ulceration only a partial keratectasia is usually produced. After parenchymatous keratitis, etc., the whole cornea protrudes.

The cicatrix is usually thinner than the normal cornea. It consists of a thick epithelial layer lying upon scar tissue, Bowman's membrane having been destroyed, at any rate in such cases as may come under microscopical observation. The fibrous tissue may undergo any of the degenerative changes which occur in anterior staphyloma, etc. Fig. 108 shows hyaline degeneration in marked degree. In this case the cornea was thickened, probably owing to the swelling of the degenerated fibres. Descemet's membrane and the endothelium persist unchanged, though pushed forwards and often wavy. When the protrusion is excessive Descemet's membrane may rupture, as in buphthalmia (Fig. 108), and, indeed, the conditions may so nearly resemble buphthalmia that an accurate diagnosis is difficult.

Conical Cornea

Conical cornea, or *keratoconus*, is a form of keratectasia. It has rarely been examined microscopically. Bowman (1859) removed an eye with this disease, and it was examined by Hulke. The portion trephined by the same surgeon in 1875 from another case was reported on by Brailey. Hulke found the central part, which was nebulous, much thinner than the periphery, and this is the experience of all operators. There was gradual thinning towards the apex. Bowman's membrane was intact, but thinned and wrinkled over the apex; Descemet's membrane was unchanged. Brailey found spaces in the superficial layers of epithelium. The pathology of the disease has been discussed by many observers, with widely divergent results. As these are purely theoretical, they merely demand enumeration: (1) Increased intra-ocular pressure (v. Graefe, de Wecker and Landolt); (2) malnutrition (Lawson, Nettleship, Swanzy, Berry, etc.); (3) diminution of the resistance of the cornea (Soelberg Wells, de Wecker and Masselon); (4) inherent weakness, and deficient firmness and thickness of the cornea (Macnamara, Williams); (5) defective embryological development and growth of the centre of the cornea (Tweedy); (6) chronic disease of Descemet's membrane and the endothelium (Panas, Elschnig); (7) relatively greater extra-ocular than intra-ocular pressure (Gullstrand), etc.

Bowman.—R. L. O. H. Rep., ii, 1859. Brailey.—R. L. O. H. Rep., viii, 2, 1875. Tweedy.—T. O. S., xii, 1892. Panas.—A. d'O., v, 1885. Elschnig.—K. M. f. A., xxxii, 1894. Gullstrand.—A. f. A., xxvi (Literaturbericht), 1892.

ŒDEMA

Œdema of the cornea was first described and investigated by Leber and Fuchs, though bullous keratitis had already been examined microscopically by v. Graefe. The condition is found most frequently in cases of increased tension, though it also occurs in panophthalmitis and many other affections. There is usually a uniform haze of the cornea, with marked dulness of the surface, which, when magnified, shows uneven epithelium. In more advanced cases minute vesicles are formed (*vesicular keratitis*), and these, especially in cases of deep



FIG. 109.—ŒDEMA AND ATROPHY OF EPITHELIUM. × 200.

Glaucoma two and a quarter years after extraction of f. b. from vitreous with Haab's magnet. The basal epithelial cells are elongated, vacuolated and separated by droplets of fluid. To the left they have disappeared, only the flattened superficial cells remaining.

parenchymatous inflammation, may increase in size and form distinct blebs (*bullous keratitis*).

Microscopically changes are found in all the layers of the cornea.

Epithelium.—In the epithelium, small drops of liquid are found at first between the basement cells, but later the channels between the prickle-cells are broadened, and ultimately the œdema extends to the superficial cells, which are loosened and often cast off (Fig. 110). In hardened specimens the fluid is coagulated in places, forming small granular clots between the cells. The fluid between the basal cells forms small droplets, which may be arranged in rows, like the beads of a rosary. The cells may be lifted up from Bowman's membrane by the fluid. In the middle layers the prickle-cells are forced apart, so that the tooth-like processes are very clearly seen, though they do not now

interlock as under normal conditions. The superficial cells are usually last and least affected. A few leucocytes are often seen between the cells.

The cells themselves also become vacuolated. The basal cells are often elongated, the basal parts containing fluid which does not stain, whilst the nuclei occupy the distal ends (Figs. 109, 116). If the swelling is great some of the cells burst and leave small depressions, which, together with the swollen and projecting cells, render the surface of the cornea uneven and lustreless (Fig. 111). This change is the usual cause of the stippled appearance in cases of glaucoma, iridocyclitis, interstitial keratitis, etc.

Sometimes the œdema affects most the middle or deepest layer of cells, or the epithelium may, by uniform swelling, be changed in some places into a nearly homogeneous mass, which soon falls off entirely. In other cases successive layers of cells are alternately swollen, the swollen layers being recognisable by the greater diameter and lighter tinge of the cells (Fig. 112). This proves successive changes in the pathological process which causes the swelling. It is probable that the changes in the epithelium described, viz., œdema and swelling, are often very transient, the liquid becoming absorbed as quickly as it is produced (Fuchs).

The liquid effused in and between the cells diminishes their coherence, so that the superficial cells fall off. This *desquamation* is never entirely absent in cases of acute corneal disease, its intensity depending on the degree and on the special character of the inflammation, being found *par excellence* in neuro-paralytic keratitis. In the slightest degrees single cells only are exfoliated; in severer cases whole layers of cells are thrown off (Fig. 113). The basal cells are then often small and cubical, staining deeply; they are young cells which have to divide so rapidly to replace the loss that they have not time to reach full maturity. After the elimination of the superficial cells the surface is usually uneven (Fig. 114), and this also may be a cause of the stippled appearance seen clinically. Rarely the surface remains smooth. If the desquamation increases it may leave behind only the basement layer of cells, which are then either short and cubical or long and thin (Fig. 115). In the latter case they are often set obliquely on Bowman's membrane, owing to the pressure of the lids. Desquamation may go so far as to lead to entire loss of the epithelium.

The effusion between and vacuolation of the deeper cells may lead to the formation of microscopic vesicles. In the same manner larger *cystic spaces* arise, between which the epithelial cells are compressed, so that they become elongated and spindle-shaped, often losing their nuclei and appearing as fibrous walls to the cysts (Klebs).

Vesicular and bullous keratitis is due to the formation of vesicles and blebs in the epithelium (Fig. 116). It often occurs after inflammation, but without direct relation to the actual infiltration (Bock). The intact vesicles are rarely seen microscopically. The walls consist of spindle-shaped epithelial cells, often projecting into the lumen, which may contain a few leucocytes or red corpuscles and granular *débris*. The larger blebs of bullous keratitis have been investigated by

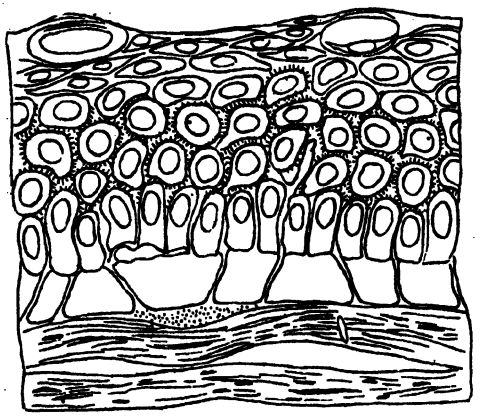


FIG. 110.—ŒDEMA OF THE CORNEA.

Fuchs, after Greeff, T. O. S., xxii. Swollen vacuolated cells on the surface; separation of the prickle-cells with fluid; drops of fluid between and beneath the basal cells; dilatation of the nerve-canals in Bowman's membrane; coagulated exudation between Bowman's membrane and the superficial lamellæ; separation of the lamellæ by fluid.



FIG. 111.—ŒDEMA OF THE CORNEA.

Fuchs, T. O. S., xxii. Vacuolation and rupture of the superficial epithelial cells, causing unevenness and stippling of the surface of the cornea.

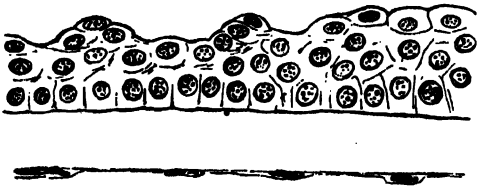


FIG. 114.—DESQUAMATION OF EPITHELIUM.

Fuchs, T. O. S., xxii. Desquamation of the superficial cells, leaving the surface uneven, causing a stippled appearance.

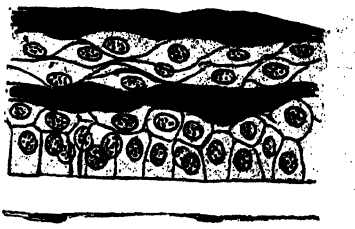


FIG. 112.—ŒDEMA OF THE CORNEA.

Fuchs, T. O. S., xxii. Œdema of alternate layers of the epithelium. The swollen cells stain less deeply.



FIG. 113.—ŒDEMA OF THE CORNEA.

Fuchs, T. O. S., xxii. Œdema of the epithelium leads to loosening of the superficial layers, resulting in desquamation. From a case of acute gonorrhœal ophthalmia, in which the cornea looked apparently normal. Note that the basal cells are small and square, due to rapid regeneration; this is further shown by their staining deeply.



FIG. 115.—DESQUAMATION OF EPITHELIUM.

Fuchs, T. O. S., xxii. All but the basal cells have been cast off. These are elongated, and are oblique, owing to the pressure of the lids. Note the erosion of the anterior surface of Bowman's membrane, the space being overfilled with scar tissue. This resembles the deposits described by Baas in old phlyctenules, but in these the erosion was from behind (*v.* p. 190).

v. Graefe, Fuchs, Schweigger, and others. They are much more resistant than the vesicles, and Fuchs attributes it to the formation of a new fibrous membrane in the anterior wall. This consists of long connective-tissue fibres with few nuclei; in one case it contained no blood-vessels, in another it was richly vascularised. The quite normal epithelium lay upon this membrane; the posterior wall of the bleb was formed by Bowman's membrane. Hess, however, never found any traces of Bowman's membrane in the wall. Treacher Collins describes the development of dense fibrous tissue between the epithelium and Bowman's membrane, the latter being broken by the extension through it from behind forwards of considerable collections of fibrous tissue. He considers that this develops in the distended spaces.

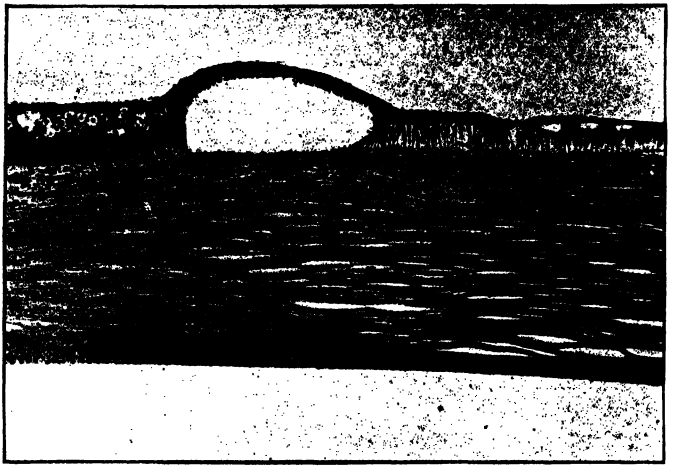


FIG. 116.—ŒDEMA OF THE CORNEA. × 60.

From a glaucomatous eye. The epithelium is œdematous; on the left the cells of the central layers are vacuolated; on the right the basal cells are elongated and vacuolated. A large vesicle is seen, the epithelium being raised by the accumulated fluid. Bowman's membrane has been absorbed as far as near the extreme right of the figure, which is towards the centre of the cornea. The lamellæ are separated by fluid except at the posterior part.

The vesicles in *herpes corneæ* (febrilis and zoster) are probably identical microscopically with those of vesicular keratitis. The occurrence of vesicles in herpes has led some authors to suppose that local nervous irritation is a factor in the production of ordinary vesicular and bullous keratitis (Birnbacher and Czermak, Panas).

Substantia propria.—Œdema of the cornea manifests itself in the substantia propria by widening the interlamellar lymph-spaces (Figs. 110, 116). The lamellæ themselves contain more fluid, and are swollen. They are separated by clefts, which are largest immediately below Bowman's membrane, and diminish in size from before backwards. The spaces contain clear fluid or granular coagula (Fig. 110), with a few leucocytes, and are often spanned by fine fibres. The corneal

corpuscles are flattened against the lamellæ, which are often wavy. There is usually a space between Bowman's membrane and the lamellæ. The perineural lymph-spaces are also dilated, and are most clearly seen where they traverse Bowman's membrane.

Descemet's membrane and endothelium.—Descemet's membrane is unchanged, but the endothelium is probably often affected. Leber has shown that fluid cannot enter the cornea from the anterior chamber as long as the endothelium is intact. Fuchs considers that the endothelium is often altered pathologically in these cases, resulting in changes in form of the cells and dilatation of the intercellular spaces, so that fluid is able to reach the cornea. It is probable from E. v. Hippel's experiments with fluoresceïn that these changes are more frequent than has hitherto been suspected (*see* "Interstitial Keratitis"). At the same time it cannot be doubted that this is only a subsidiary factor in œdema of the cornea, and that the condition depends essentially upon anomalies in the lymph circulation in the cornea itself, and this is related most intimately with the peripheral blood-vessels in the limbus (Leber, Birnbacher and Czermak).

v. Graefe.—A. f. O., ii, 1, 1853. Schweigger.—Lehrbuch der Augenheilkunde, 1873. Leber.—A. f. O., xxiv, 1, 1878. *Fuchs.—A. f. O., xxvii, 3, 1881; T. O. S., xxii, 1902. Bock.—K. M. f. A., xxiv, 1886. Birnbacher and Czermak.—A. f. O., xxxiii, 2, 1887. Klebs.—Ziegler's Beiträge, xvii, 1895. Hess.—A. f. O., xxxix, 1, 1893. Treacher Collins.—Lancet, 1900. Panas.—Leçons de Clinique opht., Paris, 1899. Stölting.—K. M. f. A., xxxix, 1901. de Schweinitz and Shumway.—A. of O., xxxii, 1903.

STRIATE OPACITY

Striate opacity, or so-called Striate Keratitis (Streifenkeratitis, Faltentrübung), of the cornea occurs under various conditions.

The lines appear sometimes as more or less straight and parallel bars of light grey opacity in the substance of the cornea; sometimes they are unbranched, sometimes they are, or appear to be, branched, or crossed by other bars running at different angles; in some cases the points of crossing of the several lines are increased in size by the formation of a nodule of opacity where the two lines come into contact. The bars, as a rule, appear to be quite solid and granular, and may reach a width of about 0·5 mm.; instead of being solid, they are occasionally seen to have a double contour,—that is to say, each line is made up of two distinct lines with a comparatively clear space between them; when this arrangement is present, the appearance is very strongly suggestive of a tubular formation in the substance of the cornea (Holmes Spicer).

Many of the cases are traumatic, and present a series of fine grey lines running from the edge of the wound towards the centre of the cornea. The traumatic variety that has excited the greatest amount of interest and provoked the greatest amount of discussion is that which is one of the commonest sequels of cataract extraction. The duration of the phenomenon varies between a few hours and several weeks.

Becker described the appearances seen in the case of a girl who had had a diabetic cataract removed by operation and died two days after; well-marked striate opacity was present before death. Microscopic examination showed a marked widening of the tissue spaces in the cornea, especially in its deeper layers; a few lymphoid cells were present, but there was no great cellular exudation.

v. Recklinghausen described the examination of another case in which there was widening of the lymph-spaces of the cornea, especially in the deeper layers.

Nuel next suggested, from clinical observation and from the examination of a cornea post mortem, the following explanation:—The whole cornea is creased or folded; on the summit of the folds the endothelium suffers a solution of continuity, and a non-inflammatory infiltration of the cornea ensues. He considered that the folds might be produced by pressure of a bandage.

This was the starting-point of another theory, first put forward by Hess, that the folds are not due to a pressure bandage, as they occur when the eye has not been bandaged. From the examination of an excised eye affected with striate opacity, and from a series of experiments on rabbits' eyes, he concluded that a widening of the corneal spaces was not present, or, if so, in the superficial layers only, and that the lines were due to a folding of the posterior layers of the cornea, including Descemet's membrane. This folding was due to the alteration in tension of Descemet's membrane, consequent upon the section.

Since then Schirmer has confirmed this view by a series of experiments on rabbits. He is of opinion that the pathological appearances shown in Becker's sections do not explain the clinical phenomena. According to Becker, there are large numbers of small lymph-spaces running in various directions through the corneal parenchyma, and crossing one another, whereas clinically we see individual streaks several millimetres long by about 0·5 mm. broad, which commonly do not cross, but run at right angles to the direction of the wound in a more or less parallel direction. Schirmer next deals with the striate opacities which appear in keratitis with hypopyon, and he thinks these are caused by folds in Descemet's membrane, for the following reasons:—By transmitted light they appear, not as opaque lines, but as clear, bright streaks; they therefore depend on a difference in light reflection. They occur at one level only, that of Descemet's membrane; they radiate from the edge of the ulcer, an arrangement which does not exist in any of the natural spaces of the corneal parenchyma. They are, therefore, clinically identical with the striæ which appear after cataract extraction.

Leber draws a strong distinction between the actual stripes and the diffuse opacity which often occurs between them. This, according to both Leber and Schirmer, is due to absorption of fluid, permitted by lesions of the endothelium of Descemet's membrane. It is found especially after difficult extractions, with considerable bruising of the cornea and the edges of the wound.

Holmes Spicer has recorded a series of cases with marked striate

opacity. He draws attention to the frequency of inflammation of the uveal tract, shown generally by iritis or by keratitis punctata. He is inclined to regard some cases as due to œdema of the posterior layers of the cornea, the arrangement of the vertical lines being possibly aided by the pressure of the lids.

Another factor in some cases is probably the contraction of cicatricial tissue, leading to folding of Descemet's membrane (Schirmer); but this will not account for the early onset in cases of cataract extraction.

I have observed a case of well-marked striate opacity, due to differences of refrangibility in an otherwise clear cornea, in a case of

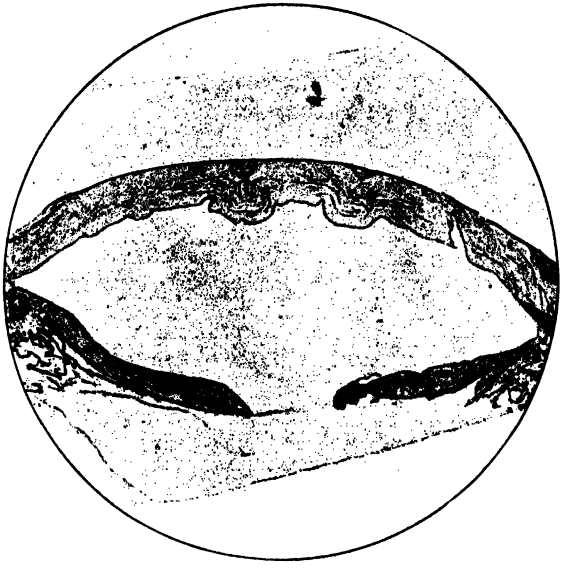


FIG. 117.—STRIATE OPACITY OF THE CORNEA. × 7.

From a case of phthisis bulbi (*see* text). Note the wrinkling of Descemet's membrane and of the corneal lamellæ; Bowman's membrane is intact and flat. There is some œdema of the substantia propria. Note the retraction of the iris and deepening of the anterior chamber.

phthisis bulbi, in which the corneal curvature was markedly increased by the shrinking of the posterior part of the eye, Descemet's membrane being thrown into folds. The appearance clinically resembled cracked ice (Fig. 117).

A totally different type of striate opacity occurs in cases of detached retina which have been treated by firm bandaging. The stripes are not parallel, but cross each other in all directions, like crumpled paper. These are said to be due to folding of the deeper layers (Nuel, Deutschmann, Fuchs).

Allied to striate keratitis is a condition found under the same conditions after cataract extraction. The opacity is uniform, or only divided into a number of square areas by fine dark lines. This opacity

cannot be caused by folding alone, but is due to imbibition. The microscope shows the lamellæ of the cornea within the limits of the swelling to be separated by effused liquid; sometimes they exhibit a very fine folding, and have grown thicker by it (Fuchs).

Schirmer has described a similar condition after injury, where, in the highly œdematous cornea, there is a central opacity divided up into irregular areas by straight dark lines, crossing each other at various angles. He calls it "thread-like" (fadenförmig) opacity, and considers it an advanced form of striate opacity.

The radial striæ described by Schirmer in hypopyon ulcer had already been pointed out in the works of Saemisch, v. Michel, Fuchs, de Wecker, and Schmidt-Rimpler. They are 2—6 mm. long, and $\frac{1}{4}$—$\frac{1}{2}$ mm. broad near the ulcer; they never branch, and are usually straight, rarely slightly wavy. As already mentioned, they depend upon differences of refraction, and are due to crumpling of Descemet's membrane and the adjacent lamellæ. They must therefore be care-

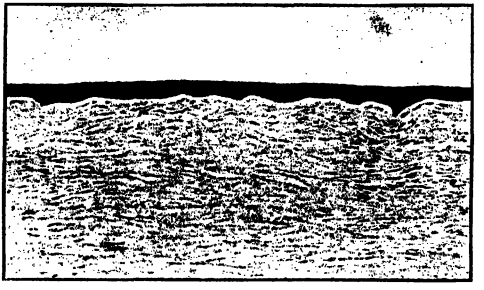


FIG. 118.—WRINKLING OF BOWMAN'S MEMBRANE. × 55.

Bowman's membrane is intact, but wrinkled. The depressions are filled in with epithelium, the surface of the epithelium being level. The condition, which is not very common, is found in some shrunken globes, and is probably due to irregular stress and strain, caused by the contraction of the posterior part of the globe.

fully distinguished from the true radiating opacities which branch, and which are due to infiltration of the lymph-spaces (*v.* p. 187).

Geometrically arranged systems of opaque lines have been described by Friedenberg, Dimmer, and others, as an unusual sequel of interstitial keratitis. They are also probably due to folding of Descemet's membrane, though Friedenberg ascribes them to deposits of fat in the lymph-spaces. Raehlmann described them in various types of secondary parenchymatous keratitis.

Schirmer has also described striate opacities in which Bowman's membrane is folded, and I have also observed these. Schirmer's case was a shrunken globe, in which the cornea was much diminished in size, hazy, and traversed by fan-like stripes, diverging above, where they did not reach the corneal margin, and ending below in a horizontal, slightly bent, grey line. In horizontal sections, there were six waves in the epithelial surface, below which were sharp triangular depressions in Bowman's membrane, which was intact (*cf.* Fig. 118).

BECKER.—Atlas der path. Topog. des Auges, plate xxx, 1878. v. RECKLINGHAUSEN.—B. d. o. G., 1887. NUEL.—Bull. et Mémoires de la Soc. franç. d'Opht., 1892. HESS.—A. f. O., xxxviii, 4, 1892; A. f. A., xxxiii, 1896. SCHIRMER.—A. f. O., xlii, 3, 1896. LEBER.—B. d. o. G., 1887. *HOLMES SPICER.—R. L. O. H. Rep., xiv, 1896. DEUTSCHMANN.—B. z. A., i, 1890. FUCHS.—T. O. S., xxii, 1902. FRIEDENBERG.—New York Eye and Ear Inf. Rep., 1895. DIMMER.—Z. f. A., v, 1901. RAEHLMANN.—K. M. f. A., xv, 1877.

FILAMENTARY KERATITIS

Filamentary keratitis (Fädchenkeratitis) sometimes occurs after abrasions, wounds, and rarely without any apparent cause. Fine filaments appear upon the cornea, 2—4 mm. long, firmly attached at one end, the free end having a knob. In idiopathic cases they are usually preceded by vesicles.



FIG. 119.—FILAMENTARY KERATITIS.

After Hess, A. f. O., xxxviii. A filament removed with forceps; the distal end is not shown.

Leber considered that coagulation products from the conjunctival sac became anchored to an abrasion, and gradually grew by accretion. He pointed out that the epithelium grows over the filament for a certain distance.

Uhthoff and Fischer regarded the filaments as fibrinous coagula derived from the fluids of the inflamed cornea, their peculiar shape being due to their inherent elasticity.

Czermak succeeded in reproducing similar bodies experimentally from mucous filaments.

Hess first completely investigated them, and his conclusions are undoubtedly correct, and can be easily confirmed. He removed them, together with the portion of epithelium from which they sprang. Here there is a triangular elevation of the epithelium, from the apex of which the filament projects (Figs. 119, 120). At the base of the triangle

a tendency to torsion is seen, which increases towards the apex. The cells, with their nuclei, become stretched out and elongated, and finally coiled into spiral fibrillæ. Nuclei are often absent, or do not stain, for a considerable distance. The neighbouring epithelium of the cornea is often pathologically altered, being vacuolated, or containing hyaline or pigmented inclusions. Groups of sixty or more nuclei may also be found heaped together. Mitotic figures are absent, and Hess attributes these abnormal groups to amitotic division, such as occurs in

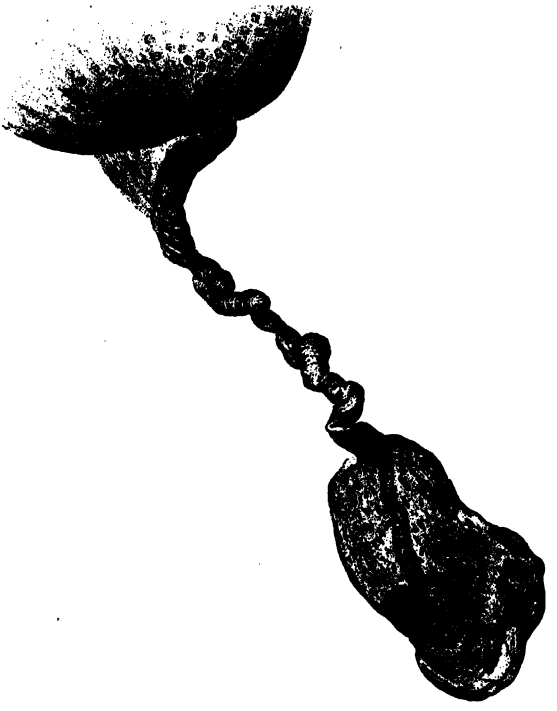


FIG. 120.—FILAMENTARY KERATITIS.

After Hess. A filament removed with a keratome; the distal end is artificially spread out, so as to show the structure.

degenerating cells. These degenerated cells often form the main part of the knob in which the filament ends. The whole is bathed in mucoid material.

The spiral arrangement is probably due to the movements of the lid. Treacher Collins has suggested that the filaments originate in the partition wall between two vesicles. As these increase in size the wall is pushed forwards, and when the vesicles burst a filament of epithelium projects from the surface.

Hess describes a different form of filament which occurs only at the site of discission wounds. These are clear, with a central core, and consist of hyaline material with a few leucocytes, but no epithelial cells. They are not attached to the epithelium, but pass deeply into the wound. They are attributed to vitreous which has been pressed forth from the puncture.

LEBER.—B. d. o. G., Heidelberg, 1882, 1889. UHTHOFF.—A. f. O., xxix, 3, 1883. FISCHER.—A. f. O., xxxv, 3, 1889. CZERMAK.—K. M. f. A., xxix, 1891. *HESS.—A. f. O., xxxviii, 1, 1892; xxxix, 2, 1893. NUEL.—A. d'O., xiii, 1893. COWELL AND GRIFFITH.—T. O. S., xiv, 1894. TREACHER COLLINS.—Lancet, 1900.

INFLAMMATION

KERATITIS IN GENERAL

Bowman (1849) first drew attention to the minute changes in the cornea in inflammation, and he was followed by Virchow (1852) and his pupil Strube (1851), His (1856), Weber (1858), Rindfleisch (1859), and Langhans (1861). At this period, only the fixed corneal corpuscles were known, and all cellular changes were attributed to them, though their dependence for nutrition upon fluid (lymph) exuded from the peripheral blood-vessels was recognised (Virchow, 1843). The discovery by v. Recklinghausen (1862) of wandering cells, resembling white corpuscles, altered the whole aspect of the subject, and the enormous increase of cells in inflammatory conditions could no longer be attributed without further proof to the corneal corpuscles. v. Recklinghausen placed pieces of cornea in the lymph-sac of a frog, and found that they were rapidly permeated with cells; and since this took place in absolutely dead corneal material, it was obvious that the cells were derived from without. Moreover if particles of cinnabar were placed in the lymph-sac, they were taken up by the cells, and were also present in the intra-corneal cells—a further proof that these had wandered into the tissue.

Cohnheim (1867—1873) showed in a series of experiments that white corpuscles leave the blood-vessels in large numbers during inflammation, and wander at large in the tissues. By marking the leucocytes with cinnabar (v. Recklinghausen) or aniline blue (Cohnheim) it was possible to demonstrate that they wandered into the cornea *in situ*, in the same manner as into the dead cornea in the frog's lymph-sac. Cohnheim went too far in denying any activity in the corneal corpuscles, an opinion which met with vigorous and insufficiently restrained opposition from Stricker, Böttcher, and others.

Eberth (1876) paid special attention to the part played by the corneal corpuscles in regeneration, which was also investigated by Senftleben (1878), who considered that the corpuscles only reproduced themselves, and never gave origin to pus-corpuscles. Ranvier thought that the function of the leucocytes in corneal wounds was to afford nourishment to the proliferating corneal cells.

Stricker had already asserted the activity, not only of the corneal cells, but also of the ground substance; and Heitzmann affirmed the presence here of living material which, during inflammation, returned to an embryonic cellular condition. Grawitz went so far as to assert the presence of "sleeping" cells, which awoke to activity under the stimulus of inflammation, and became manifest as lanceolate figures (Spiessfiguren, *vide infra*), much as crystals are formed from a solution. His suggestions and criticisms of earlier work met with great and successful opposition from Klemensiewicz, Yamagiva, Orth, Lubarsch, Schnaudigl, and others.

Meanwhile the bacteriological aspects of the subject had been investigated, first by Nassiloff (1870), later by Eberth (1873), Orth (1873), Leber (1891), and others. Leber's experiments on mycotic keratitis produced in rabbits by aspergillus were especially productive of results from the morphological standpoint. Finally, Councilman (1899) has thrown much light upon the characters of the wandering cells. He has shown that fifteen minutes after central infection of the cornea with staphylococci granular leucocytes are found in the conjunctiva; these are also the first to appear in the cornea, and form the majority of the wandering cells. In eighteen to twenty-four hours isolated non-granular leucocytes are found in the peripheral part, and in four days, lymphocytes. The latter occur only in the lymph-channels at the periphery, and probably come from lymphatic glands, and not from the blood. After five days plasma-cells appear in the outer third of the cornea. These and the lymphocytes show mitotic figures, which are absent in the other wandering cells.

It will be seen, therefore, that the cornea was early recognised by general pathologists as specially adapted for the investigation of the fundamental processes which go on in all cases of inflammation. All kinds of animals (frog, fish, birds, guinea-pig, rabbit, dog, etc.) and all sorts of stimuli (suture in the cornea or bulb, cauterisation—thermal or chemical,—inoculation of bacteria or moulds, etc.) were used. The first effect is a grey opacity at the site of injury, appearing in a few hours, and rapidly followed by hyperæmia at the limbus, doubtless due to the irritating effect of soluble products carried outwards by the lymph-stream. The reaction is most rapid with bacterial inoculations. The second, less constant effect is a peripherial opacity, most marked near the primary injury, but involving the whole circumference when this is central, though here it is most marked above and below. It is a prominent feature in *induced keratitis*, where the original focus lies in the anterior chamber or some other part of the eye; it then often involves the whole cornea. When the injury is central, the peripheral opacity may clear up from the outside, leaving a dense *infiltration ring* around the central focus. This is caused, according to Leber, by positive chemotaxis. At the site of inoculation, the organisms increase and cause death of a limited area of the tissue, owing to the concentration of the toxins. Diluted toxins diffuse to the periphery of the cornea, and lead to hyperæmia with increased permeability of the vessel walls to plasma, and emigration of leucocytes. The latter are attracted by positive chemotaxis to the focus of irritation. Before they

reach the necrotic area, however, and at a variable distance according to the virulence of the organisms, the leucocytes are paralysed and die. Here they accumulate and form the infiltration or migration ring. They wage war upon the bacteria in two chief ways: (1) directly upon any outlying organisms by phagocytosis, and upon their toxins by counteracting chemical products; (2) upon the necrotic tissues by forming pepsin-like ferments which dissolve these and thus facilitate their removal mechanically into the conjunctival sac, and by absorption into the lymph-stream. There are also leucocytes in the central area, but these are derived directly from the conjunctival sac. Owing to the flatness of the cornea and the arrangement of the laminæ the migra-



FIG. 121.—KERATITIS. × 120.

Oblique section, to show corneal corpuscles and infiltration with leucocytes. The epithelium is seen above.

tion zone is rather a ring than a cup, but this is notably influenced by details, as we shall see in treating of hypopyon ulcers (q. v.).

On account of the multiplication of the organisms in the lymph-channels between the corneal lamellæ in cases of acute infection, where the protective migration of leucocytes is inefficient, fine grey radial stripes with straight branches can often be made out with a corneal *loupe*. Similarly the outer edge of the infiltration zone fades off, owing to the diminishing concentration of the toxins, in less acute cases.

Microscopically the leucocytes and corneal corpuscles are much altered by their position between the lamellæ, etc., so that they are no longer easily differentiated, especially in vertical sections. In tangential sections the more deeply staining nuclei of the leucocytes distinguish them from those of the fixed cells, though the degeneration of the latter often leads to their nuclei becoming round and taking up the stain

unusually well. The wandering cells lie in the lymph-spaces between the lamellæ and around the nerves, and also between the fibrils inside the lamellæ. They are therefore compressed into long, straight, spindle- or lance-shaped figures, which may be called *inflammatory spindles* (Entzündungsspiesse). These are often marshalled in parallel rows, which cross one another at various angles (Fig. 122). Owing to the compression to which they are subjected, the polymorphic nuclei are characteristically altered, and little resemble their usual form. They appear—though it is probably merely an appearance—to be broken up into round, oval, and very frequently club-shaped masses, which are less often in the middle of the cells than at the poles. Many are united by extremely fine drawn-out filaments; others seem to be

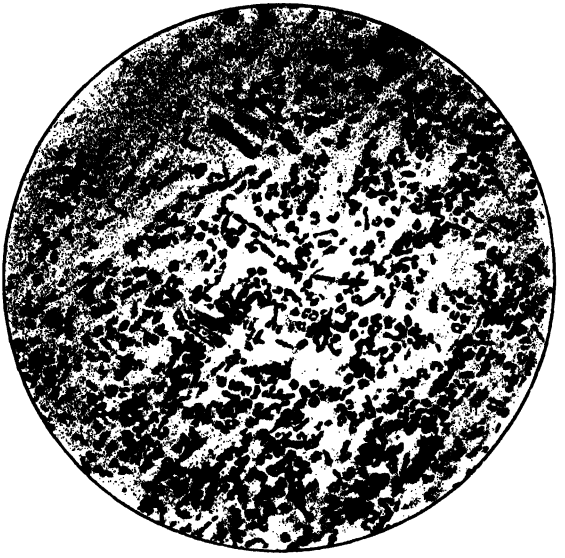


FIG. 122.—KERATITIS. × 180.

Oblique section from same specimen as Fig. 121. The nuclei of the corneal corpuscles (faintly stained) and of the leucocytes are seen; many of the latter show the arrangement of inflammatory spindles.

isolated. The nuclear masses and filaments are very rich in chromatin, and stain very intensely with nuclear stains. The cytoplasm contains granules, which are generally neutrophile (especially in the rabbit), occasionally eosinophile (especially in the pigeon), and this demonstrates their leucocytic nature (Schnaudigl). The granules are shown in frozen sections of fresh tissue stained for half a minute with Ehrlich's triacid mixture, or in hardened tissue stained by hæmatoxylin and eosin; in the moist chamber amœboid movements have been observed in the cells (Orth).

The leucocytes are derived from two sources: (1) those normally present in the cornea, reinforced during inflammation by others which have emigrated from the peripheral vessels; (2) those which have made

their way in from the conjunctival sac. The latter enter chiefly where the epithelium is lost, and in less degree where the epithelial cells are more or less degenerated and separated from each other; they show little tendency to invade the intact epithelium. Descemet's membrane is a complete bar to their progress, so that none are derived from the anterior chamber, nor do intra-corneal leucocytes contribute to hypopyon. Most of the cells are polymorphonuclear cells, though other leucocytes are also found, as well as lymphocytes.

The corneal corpuscles are, for the most part, easily distinguished from the leucocytes: (1) the nuclei are round, oval, curved, or horse-shoe-shaped; (2) they are larger; (3) they stain more faintly with nuclear stains; (4) there are no colourable granules in the cytoplasm; (5) they often show mitotic figures. Round leucocytes often lie in the concavity and elsewhere in the neighbourhood of the fixed cells, but separated from them by a clear zone. They are best seen in gold-chloride preparations, in which the cytoplasm of the corneal corpuscles is stained (Orth). Other corpuscles, especially near the primary focus, show degenerative changes—swelling, vacuolation, fatty degeneration, or complete necrosis. Under these conditions fragmentation of the nuclei may occur, so that appearances of multinuclear cells arise (Böttcher), though it is doubtful if these are not leucocytes.

The ground substance of the cornea probably plays a purely passive part, for the active changes described by Stricker, Heitzmann, and especially Grawitz cannot be considered proved, and are unlikely on general principles. The lamellæ are forced apart by increased exudation, and their constituent fibrillæ are separated by leucocytic infiltration. Chemical changes follow, partly due to the action of toxins and partly to the ferment action of the leucocytes, resulting in softening and solution.

The first evidence of repair is seen in the development of new vessels from the part of the limbus lying nearest to the focus, or, when this is central, from the whole periphery. Their chief function is that of supplying the necessary material for making good the loss of substance. They lie in the most superficial layers of the cornea, between the epithelium and Bowman's membrane; but in severe or prolonged inflammations they are also formed beneath Bowman's membrane. They are at first mere endothelial tubes, accompanied by a small amount of granulation tissue, including, according to Orth, fibres which stain with elastic-tissue stains. They may ultimately atrophy, forming fine, solid, cellular threads; or some may remain permanently, developing a definite adventitia.

Other signs of regeneration are seen in the mitotic division of the corneal corpuscles, from which the scar tissue is formed, though the plasma-cells may take part in the process. Long spindle-shaped cells or *regeneration spindles* (Regenerationsspiesse, Senftleben) are formed, often with many thick processes. The scars after many inflammatory conditions differ from those after wounds in being more fibrous, the cells being smaller and more compact, with deeper staining, more rod-like nuclei. Regeneration of the epi- and endo-thelium takes place by karyokinetic division of the cells.

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PHLYCTENULAR KERATITIS

Phlyctenular keratitis has been examined microscopically even more rarely than the same form of conjunctivitis, of which it is merely an extension. It affects the superficial layers of the cornea, which correspond morphologically with the conjunctival layer, though whether the anterior layers of the substantia propria are of conjunctival origin is doubtful, and not very probable.

Iwanoff (1869) found nodules of cells upon Bowman's membrane, raising the epithelium; they also surrounded the nerve-fibrils passing through this membrane, which might be partially destroyed. The infiltration around the nerves was held to account for the pain and photophobia.

Leber and Wagenmann (1897) confirmed the presence of subepithelial nodules; the epithelium was infiltrated and ultimately destroyed, and superficial vascularisation occurred.

Baas found nodules below Bowman's membrane in a case of prolonged scrofulous keratitis with superficial opacities. The nodules consisted of new-formed fibrous tissue, with flattened nuclei lying parallel to the surface; they involved either the whole or only the deeper part of Bowman's membrane, having either a broad basis of attachment to the substantia propria or a narrow pedicle (*cf.* Fig. 115). These nodules were obviously late scars, and but little stress can be laid upon the observations, especially as the patient was also syphilitic, and had specific choroiditis. So far as they go they tend to show that the phlyctenules are endogenous, the aggregations of leucocytes lying originally below Bowman's membrane.

The cases reported by Gruber and Hertel are even more open to question. The first was in a child aged two and a half months, and was a deep purulent ulcer; the second was in a shrinking eye with leucoma adhærens. In the latter the changes were also beneath Bowman's membrane, which was fibrillar and broken through in places.

The site of the phlyctenules was marked by dense infiltration, the epithelium being lifted up and partially destroyed. There were several small subepithelial nodules in the conjunctiva.

Augstein reported the case of a child with pannus scrofulosus and multiple infiltrates in the cornea. There was infiltration and formation of new connective tissue in the superficial lamellæ. Bowman's membrane was to a large extent destroyed. Vessels were found both in the superficial layers and deep in the cornea.

Seo and Yamaguchi, in a case of fascicular keratitis and pannus scrofulosus (q. v.), found small deposits of fibrous tissue and connective-tissue cells lying under Bowman's membrane, which was eroded, in the otherwise normal parts of the cornea. The most superficial lamellæ were either intact or somewhat thinned. These were doubtless the sites of former phlyctenules, and confirm Baas's results.

Very little stress can be laid upon such cases as these, and we must await the opportunity of examining an early uncomplicated case before the pathological anatomy of phlyctenular keratitis can be settled.

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Interstitial Keratitis

Interstitial or parenchymatous inflammation of the cornea, in the pathological sense of the term, is extremely common in a great variety of cases. The cases of true interstitial keratitis, in the restricted clinical sense, which have been examined microscopically are very few, and are mostly complicated by other conditions which make it difficult to determine the exact anatomy of the disease. Even amongst the cases examined, a large proportion of those described as parenchymatous keratitis were undoubtedly tubercular. This raises the question of the true ætiology of the disease. In England we are accustomed to regard the typical condition as of syphilitic origin, and no satisfactory proof has been brought forward that this view is incorrect. The same unanimity of opinion does not, however, prevail upon the Continent. The cases of Bürstenbinder, Zimmermann, and Schultze will therefore be eliminated from this section, and considered under "Tubercle of the Cornea" (q. v.).

Almost all the cases of syphilitic interstitial keratitis occur in youth in the subjects of congenital syphilis. It is found, however, rarely in acquired syphilis (Wordsworth, Lang, Juler, Lawford), and is then nearly always limited to one eye (Lawford). Valude has collected forty cases. Both in congenital and acquired syphilis it occasionally takes the form of an *annular or disciform keratitis* (Fuchs, Paukstat). Cases of delayed congenital interstitial keratitis, coming on in adult life, also occur; they are also more commonly unilateral than the usual type. A deep localised interstitial deposit may also occur in acquired syphilis; it may possibly be gummatous. In a case recorded by Nettleship it disappeared in eight months under treatment.

There is also a difference of opinion as to the cases of true interstitial keratitis. v. Michel and others distinguish between a primary and a secondary interstitial keratitis. In the former a triangular opacity appears at the margin of the cornea and gradually spreads over the whole area; it is often followed by iritis, keratitis punctata, etc., and is ascribed by v. Michel to syphilitic affection of the marginal loops of blood-vessels. The secondary form is distinguished by marked inflammation of the uveal tract, and often of the sclerotic, more particularly in the anterior part of the eye.

Leber and his pupils regard the disease as invariably secondary, following uveitis. The frequency with which anterior choroiditis can be observed ophthalmoscopically in the less affected eye in these cases is

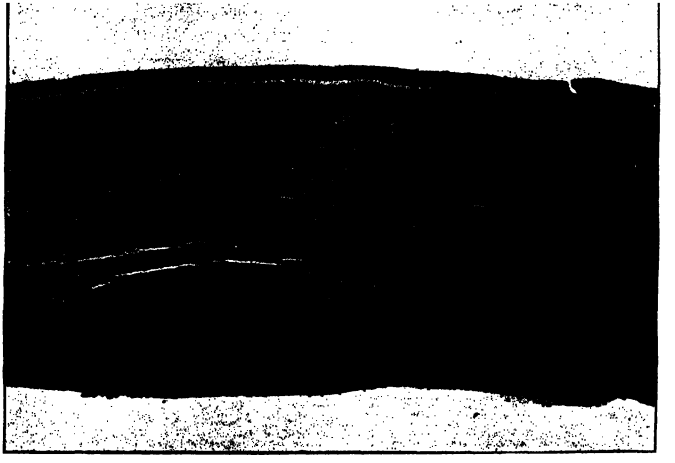


FIG. 123.—INTERSTITIAL KERATITIS. × 60.
From a specimen by Hancock. The infiltration is densest in the posterior layers.

strong evidence in favour of this view, which is further supported by such microscopical details as are available.

Most observers have found the principal changes in the deepest layers of the substantia propria (Krückow, Meyer, Fuchs, E. v. Hippel) (Fig. 123).

Krückow found many new-formed vessels here, and evidences of degeneration of the corneal corpuscles—diffuse staining, swelling of the nuclei, and contraction of the processes.

Meyer found thickening of the whole cornea, infiltration of the deep layers with round and polygonal cells, often massed together, vascularisation of the same area, and thickening of the endothelium on Descemet's membrane. The iris and sclerotic showed infiltration, lymphocytes being grouped into nodules in the iris, but there were no giant-cells. This condition is not uncommon, quite apart from any question of tubercle.

Fuchs describes similar appearances: dense infiltration of the most posterior layers of the cornea, so that they sometimes appear as if transformed into granulation tissue; numerous newly formed blood-vessels in the posterior and middle layers. The infiltration at the margin of the cornea is continued into the ligamentum pectinatum, the iris, and the ciliary body. Fuchs has also found nodular aggregations of lymphocytes. There were accumulations of leucocytes upon Descemet's membrane, but hypopyon is extremely rare.

E. v. Hippel gives an exhaustive account of two eyes. The cornea varied in thickness from 0·6 to 0·66 mm., the surface being undulating. There were leucocytes between the basal epithelial cells, and upon Bowman's membrane, which was normal except at the periphery, where there was a layer of vascular connective tissue. The whole substantia propria showed changes, which were most marked in the deep layers and near the angle of the anterior chamber. These consisted in fibrillation of the lamellæ, dilatation of the interlamellar spaces, infiltration with round-cells, and vascularisation of the deep layers and the peripheral zone. The endothelium was intact. There were tubercle-like nodules in the peripheral and deepest parts of the cornea, invading the angle of the anterior chamber and infiltrating the ligamentum pectinatum iridis. These contained several typical giant-cells, surrounded by epithelioid cells and an outer zone of round-cells. There were two giant-cells on Descemet's membrane. There was marked inflammatory infiltration around the anterior ciliary vessels. A notable feature was the extensive inflammation of all parts of the eye, especially in the neighbourhood of the ciliary vessels, so that v. Hippel regards the condition as a slight chronic panophthalmitis. It may well be doubted whether this case was not in reality tubercular.

Similar cases have been described by Wagenmann and Baas.

Rare cases of ulceration of the cornea in severe attacks of interstitial keratitis have been recorded (Treacher Collins).

An attempt has been made to reproduce the condition experimentally. Infiltration of the cornea follows various injuries to the eye, as we have already seen, and Raehlmann has paid special attention to the proliferation of the corneal cells after insertion of a suture into the sclerotic. Others have produced infiltration by injury of the endothelium, on the lines of Leber's researches. Samelsohn, for example, injected ammonia solution into the anterior chamber. Mellinger and Bärri conclude that interstitial keratitis is due to changes in the endothelium, but the condition produced by such experiments is transitory, and disappears when the endothelium recovers. It is doubtless due, as pointed out by Leber, primarily to œdema, though transient inflammatory infiltration may follow. Wagenmann and Siegrist produced a parenchymatous infiltration of the cornea by section of both long ciliary and some of the short posterior ciliary vessels. It commenced at the margin and spread rapidly over the cornea, which was swollen and œdematous. The endothelium suffered severely, being almost entirely thrown off in one case. The lamellæ were swollen and permeated by coagulable fluid, which formed fibrinous networks, especially at the periphery. Infiltration with round-cells and vascularisation

followed, undergoing retrograde changes later, and giving place to proliferation of the corneal cells and thickening of the fibrillæ. These changes are probably to be referred to the œdema following loss of endothelium, itself brought about by malnutrition. None of the experiments can be regarded as affording typical examples of the clinical form of interstitial keratitis, the immediate cause of which is yet to seek.

That changes occur in the endothelium in interstitial keratitis is rendered probable by E. v. Hippel's fluoresceïn experiments, since deep staining frequently occurs in these cases (*see also* Bihler, Benson, Gräflin).

Interstitial keratitis sometimes follows experimental thyroidectomy in animals, as I have observed elsewhere. The condition has been discussed by Gley and Rochon-Duvigneaud. It is not uncommon in dogs after distemper, and is a source of trouble in hunting packs. It has also been observed in pheasants (Treacher Collins) and in wild animals kept in captivity, *e. g.* bears (Nuel).

The formation of new vessels in interstitial affections of the cornea has received attention from Straub. They often arise in cases of experimental infection of the vitreous. Straub considers they are due to a "vaso-chemotactic" influence—which is little more than expressing the fact of their occurrence in other words.

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PANNUS

Pannus is a term which is often used loosely for any vascularisation of the cornea; it should be reserved clinically for the special types found in phlyctenular conjunctivitis and in trachoma, the latter being the more characteristic. In each case there is not merely a development of new vessels in the cornea, but an ingrowth of granulation tissue from the limbus. Opinions differ as to the exact situation of the ingrowth.

In phlyctenular conjunctivitis three types of vascularisation may occur: (1) the vascularisation of an ordinary ulcer (q. v.); (2) the *vascular fasciculus* (Fischer), which is associated with an advancing ulcer, and in which the vessels lie in a depressed furrow representing the cicatrised path of the ulcer; (3) *pannus scrofulosus or eczematosus*, in which there is a continuous new formation of tissue upon the surface of the cornea, developing from any spot upon the corneal margin. In (1) and (3) the condition may clear up completely, leaving no opacity

behind; under these circumstances the vascular tissue is superficial to Bowman's membrane. In (2) usually, and in (1) and (3) frequently, a permanent opacity is left, and it is probable that here Bowman's membrane is destroyed, either by erosion from the surface and invasion of the superficial corneal laminæ, or perhaps by primary invasion of the superficial laminæ and secondary erosion of Bowman's membrane (Baas).

In **pannus scrofulosus** Baas found an ingrowth of vascular granulation tissue immediately beneath Bowman's membrane, which showed fibrillation and erosion from beneath, resulting in places in complete destruction. He regards the condition as merely a superficial extension of the usual disseminated phlyctenular process, and as good evidence of the endogenous nature of the process. This view is largely discounted

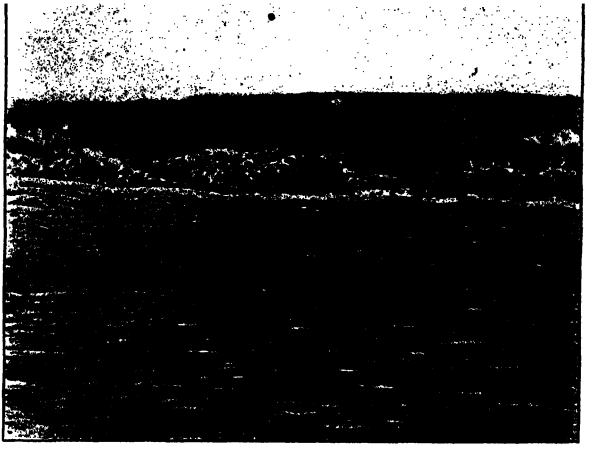


FIG. 124.—PANNUS DEGENERATIVUS. × 90.

From a case of glaucoma. Note vessels and granulation tissue between the degenerated epithelium and the intact Bowman's membrane. The substantia propria is infiltrated, and towards the periphery vascularised.

by the clinical cases in which no opacity remains; these have not yet been submitted to histological examination. It is more probable that the deeper invasion is secondary. In the later stages the cells become spindle-shaped and more densely packed, many of the vessels being obliterated, sometimes by hyaline degeneration.

Seo and Yamaguchi exhaustively investigated a case of keratitis fascicularis and pannus scrofulosus in a tubercular child æt. 2¼. In the area of infiltration Bowman's membrane and the anterior lamellæ were destroyed, and replaced by vascular granulation tissue, upon which lay the new-formed epithelium. The advancing edge of the new tissue burrowed under Bowman's membrane, eroding it from behind. The deeper layers of the substantia propria were also affected; there were deep-lying vessels surrounded with leucocytes, and there was a thick

aggregation of round-cells lying upon the anterior surface of Descemet's membrane, resembling the "posterior abscess" of hypopyon keratitis.

The cases examined have been late and severe cases. In all probability the earliest vessels and granulation tissue of the ordinary vascular fasciculus make their way between the epithelium and Bowman's membrane, and may retrogress without permanent injury to the cornea. Anatomical proof is as yet lacking.

Pannus degenerativus (Baas) is a term applied to a form of superficial pannus which occurs in blind, degenerated eyes, such as result from cyclitis, glaucoma, detached retina, etc. Here there is a growth of highly vascular granulation tissue immediately beneath the epithelium and lying upon Bowman's membrane, which is usually intact, but often

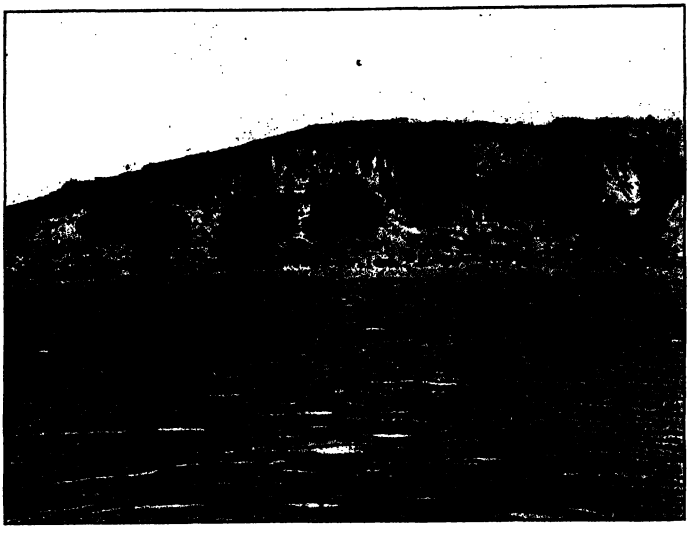


FIG. 125.—PANNUS DEGENERATIVUS. × 120.

From the same case as Fig. 124. Note the degenerative and œdematous changes in the epithelium and the large islands of epithelium lying in the granulation tissue.

folded (Fig. 124). Around the plexus of fine, dilated vessels are numerous lymphocytes, which later disappear, giving place to spindle-shaped cells, which gradually become more and more compact, with simultaneous obliteration of the finer vessels. Still later, there is extensive hyaline degeneration, with more or less complete disappearance of nuclei. The epithelium is usually thickened, and shows degenerative changes; islets of epithelial cells are seen in the midst of the homogeneous material in sections, being probably irregular processes cut across (Fig. 125). The epithelial cells are often vacuolated, or contain fatty globules, and are frequently epidermoid in the superficial layers. The homogeneous material may be flat, but more commonly is wavy upon the surface. Bowman's membrane may also be eroded and

destroyed in these cases, and the substantia propria often shows vascularisation and other changes due to the glaucoma, etc.

Pannus degenerativus is naturally the form which has most often been examined. It was first described by Müller, and afterwards by Donders, Althoff, Iwanoff, and others, and was figured in Pagenstecher and Genth's Atlas.

In **pannus trachomatosus** the new-formed tissue starts as usual at the limbus, but always in the upper part, and extends over the cornea. In the recent stage it is thin—*pannus tenuis*, and often very vascular—*pannus vasculosus*. If it has acquired considerable thickness it is called *pannus crassus* or *carnosus*, the extreme condition being sometimes called pannus sarcomatosus, a term to be avoided. An old pannus with much

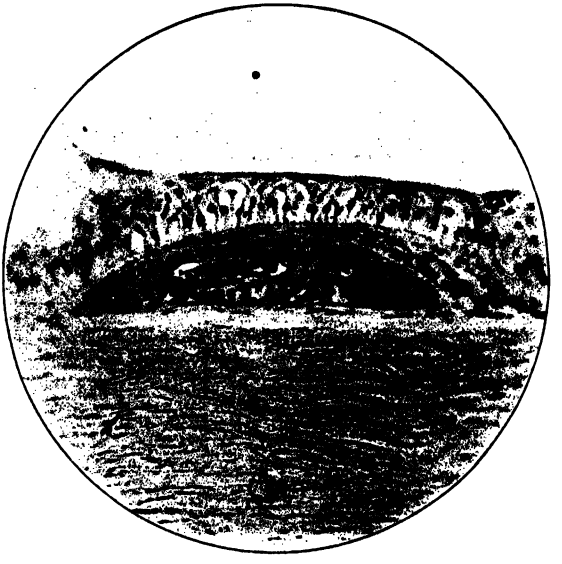


FIG. 126.—PANNUS DEGENERATIVUS. × 120.

From an eye, blind ten years, with detached retina, dislocated lens, etc. Note the laminated mass of epithelium, over which the ordinary basal cells pass, the surface being kept fairly level by degeneration of the mesial layers of prickle-cells. Bowman's membrane appears to split at the edges of the lens-shaped mass. Many polymorphonuclear leucocytes are seen amongst the epithelial cells.

cicatricial tissue and few vessels is called *pannus siccus*. Occasionally a dense white or yellow scar is formed, resembling a leucoma, but confined to the superficial tissues; or small white spots appear in the pupillary area, close to the delicate blood-vessels (Fuchs). These also are superficial, and may be removed by scraping. In progressive pannus the opacity extends beyond the vessels, which run vertically downwards, parallel to each other, without anastomosing. In the regressive stage, the vessels extend a short distance beyond the opacity. Pannus may involve the whole cornea, and in these cases the vessels enter from all sides, anastomose with each other, and often have varicose dilatations.

Pannus trachomatosus is not caused through continuity, since the

conjunctiva bulbi is usually normal, but by contiguity with the affected lid. It is not merely due to the roughness of the lid, since the same amount of roughness may be present in other diseases without producing pannus. The limbus is the most vascular part of the bulbar conjunctiva, and is therefore most apt to be inflamed. The inflammation spreads centripetally into the cornea, owing to the prevalent direction of the blood- and lymph-streams. The inflammation is induced by continual contiguity with the diseased lid, since the upper part of the cornea is covered by the lid both by night and by day. The roughness doubtless contributes to the infection by producing minute epithelial abrasions, etc.

Pannus trachomatosus is capable of complete retrogression, so that the cornea can re-acquire its normal transparency. This is strong evidence that in the early stages the vessels are insinuated between the epithelium and Bowman's membrane, leaving the latter intact. This stage rarely comes under observation microscopically, but is described and figured by Fuchs; but whether the description and figure were derived from a case of trachoma can only be inferred. If so, it in every respect resembles the early stage of pannus degenerativus.

The later stages are best described by Raehlmann, who has had unusual opportunities of investigating trachoma in all its forms. He found the epithelium normal, and even free from infiltration by leucocytes, except quite late. Bowman's membrane was also intact, though more obviously fibrillar than normal, and all the pathological changes were beneath it. Here there was great infiltration of the substantia propria with lymphocytes, which were most closely packed, and penetrated deepest into the tissues at the upper part, gradually fading off, and implicating only the superficial layers as the centre of the cornea was approached. Penetrating the upper part of this area were numerous new-formed vessels, many of the capillaries having no recognisable walls, other vessels having merely an endothelial wall, sometimes covered by a thin coating of connective tissue. The direction and distribution of these vessels has been already mentioned.

The actual substantia propria could scarcely be recognised, the laminæ being separated and split up into fibrillæ by very dense lymphocytic infiltration. The addition of these foreign elements leads to thickening of the cornea, so that the normal furrow at the periphery is absent. In places Raehlmann found nodular aggregations of lymphocytes, resembling follicles, and in every respect similar to the trachomatous nodules of the conjunctiva. These tended to invade Bowman's membrane and the epithelium, which were raised over them; and this condition might be so pronounced as to cause considerable heaping up of the tissue, so that the normal furrow was not only filled in, but actually replaced by a swelling. In these more advanced cases Bowman's membrane was destroyed, and replaced by a layer of adenoid tissue, consisting of a fibrillar network containing lymphocytes, richly supplied with blood-vessels. The epithelium was then also invaded by wandering cells. The tissue therefore tends more and more to assume the character of trachomatous conjunctiva, and pannus trachomatosus must be regarded as an invasion, not only of simple granulation tissue,

but also of specific trachoma follicles. The infiltration of the epithelium leads to its being loosened and often cast off, or rubbed off by the rough lid. Hence ulcers frequently occur, generally at the free border of the pannus, more rarely elsewhere. Fragments of Bowman's membrane may remain, but it is for the most part reduced to a fine basement membrane, or even this may disappear, the cylindrical epithelium lying directly upon the adenoid tissue. There are naturally more follicles at the limbus, but they are also found towards the central part of the cornea.

As already mentioned, the pannus may entirely disappear, leaving a clear cornea. In the more severe cases cicatrisation takes place, commencing in the neighbourhood of the vessels. The round-cells slowly diminish in number, and are seen to lie between long fine fibres, which apparently fuse into thicker homogeneous laminæ, amongst which there are a few fixed spindle-cells.

In pannus of long duration the deeper layers consist of these cicatricial sclerosed lamellæ, whilst the superficial layers are still adenoid and contain follicles, and the epithelium is studded with mucous cells in all its layers. Ultimately the whole of the adenoid tissue and infiltration disappear.

MÜLLER.—Gesammelte Schriften, I, Leipzig, 1872. DONDERS.—*See* ALTHOFF. RITTER.—A. f. O., iv, 1, 1858. ALTHOFF.—A. f. O., viii, 1, 1862. IWANOFF.—Klin. Beobacht. aus d. Augenheilanstalt zu Wiesbaden, iii, 1866. RAEHLMANN.—A. f. O., xxiii, 3, 1887. * BAAS.—K. M. f. A., xxxviii, 1900. BIETTI.—Ann. di Ott., xxxi, 1902; K. M. f. A., xli, Beilageheft, 1903.

SYPHILIS

Interstitial keratitis is described elsewhere (*v.* p. 191). Other syphilitic affections of the cornea—gummatous, etc.—have not been examined microscopically. Extension of gummatous cyclitis and scleritis into the cornea and anterior chamber have certainly been observed (*e. g.* Parsons), but there are no differential characteristics. The corneal lamellæ are swollen and œdematous, and are separated by infiltrating plugs of round-cells, which also intrude themselves between the fibrillæ of the lamellæ. The whole tissue is softened and necrotic, staining more or less diffusely.

PARSONS.—T. O. S., xxii, 1902; R. L. O. H. Rep., xv, 3, 1903.

TUBERCLE

Tubercle of the cornea is nearly, if not quite, invariably a secondary extension from the uveal tract. The posterior layers of the cornea are associated embryologically with the uveal tract, hence it is not surprising that the disease sometimes assumes the typical features of the clinical form of interstitial keratitis. Cases of this type have been examined microscopically by Bongartz, Bürstenbinder, Zimmermann, Schultze, and others (*see* "Tubercle of the Iris"). Other cases assume the form of a sclerosing keratitis, whilst yet others appear as deeply situated discrete opacities (Hartridge and Griffith).

Haensell, in 1879, produced an eruption of tubercles in the corneæ of rabbits and guinea-pigs by inoculation. He doubts, however, the existence of primary tuberculosis of the cornea, and in some experiments upon rabbits in which I inoculated the cornea with virulent cultures, I failed to obtain any result unless the anterior chamber was inoculated. The rabbits have been kept over two years and are still quite healthy. At the same time rare clinical cases favour the view that primary tubercle of the cornea does occur. The question is one of extreme importance, and merits further research. Bach describes primary tubercle in the form of nodules at the limbus or in the most peripheral parts of the cornea itself. They slowly invade the cornea, leaving, after healing, a greyish-white tongue-like opacity. Greeff records primary tubercular ulceration of the cornea from auto-inoculation by the finger-nail of a tuberculous patient. It slowly enlarged, with strong vascularisation, showing no tendency to heal, thus resembling the torpid vascular ulcers of the cornea in the presence of lupus of the face.

The cornea, however, is a bad culture medium for the bacillus, which can scarcely ever be found in the lesions. The parenchymatous type is attributed by Bach to the action of the toxins. Proof of the tubercular nature of the complaint can only be afforded by inoculation of the rabbit's anterior chamber, even histological examination rarely affording decisive diagnosis.

In Hartridge and Griffith's case the cornea was infiltrated near its posterior aspect and just within Descemet's membrane by small, round, deeply staining cells; vessels were seen penetrating this tissue. At one place near the centre there was an interruption of Descemet's membrane, and fibro-cellular tissue connected the substantia propria with a similar tissue occupying the pupillary area. The diagnosis rested upon the presence of typical tubercle systems in the iris, ciliary body, etc. The case of Bongartz was similar—caseation was absent, but tubercle bacilli were demonstrated.

In other cases there were aggregations of epithelioid and giant-cells, without caseation, between the lamellæ, and especially along Descemet's membrane (*Z*immermann). In *Z*immermann's case there was round-celled infiltration throughout the cornea. Bacilli were demonstrated in the corneal tubercles as well as in other parts of the eye.

Baumgarten's case was very advanced, and showed extensive caseation. The whole cornea was transformed into a mass of caseating tubercles, with granulation tissue. Descemet's membrane was perforated in several places, and the tissue was here continuous with the iris. It was proved clinically that the disease was an extension from the conjunctiva.

In Schultze's case there was a tubercle containing bacilli in the angle of the anterior chamber. Probably E. v. Hippel's cases (*v.* p. 193) belong to the same category.

The differences observed in the cases doubtless depend upon many factors, especially the number and virulence of the bacilli, the stage of the disease, and above all the relative inertness of the tissue. Schieck has confirmed the earlier experiments of Baumgarten upon rabbits,

which show that groups of epithelioid cells occur at the site of inoculation, but that these are liable to be covered over and obscured by lymphoid cells.

BAUMGARTEN.—A. f. O., xxiv, 3, 1878. HAENSELL.—A. f. O., xxv, 4, 1879. *PANAS AND VASSAUX.—A. d'O., v, 1885. BONGARTZ.—Inaug. Diss. Würzburg, 1891. STRUBELL.—Inaug. Diss. Würzburg, 1894. HEYDEMANN.—Inaug. Diss. Greifswald, 1894. HARTRIDGE AND GRIFFITH.—T. O. S., xv, 1895. DENIG.—A. of O., xxvii, 1898. BÜRSTENBINDER.—A. f. O., xli, 1, 1895. ZIMMERMANN.—A. f. O. xli, 1, 1895. SCHULTZE.—A. f. A., xxxiii, 1896. SCHIECK.—Ziegler's Beiträge, xx, 1896. BACH.—A. f. A., xxxii, 1896.

LEPROSY

The eyeball is very frequently attacked in leprosy. The cornea is always attacked secondarily, since it contains no vessels (Lie). Three types of inflammation are found here, a superficial punctate and a deep parenchymatous keratitis, and the formation of granulomatous tumours.

In the *superficial punctate keratitis*, small grey nodules are found under the epithelium at the periphery, and they gradually spread towards the centre. They consist chiefly of aggregations of lepra bacilli, and bacilli may be found free in the lymph-spaces, with or without proliferation of the neighbouring cells (Neisser, Lie, Uhlenhuth). Lie was unable to find mitoses in the corneal corpuscles, the inflammatory cells consisting chiefly of polymorphonuclear leucocytes and endothelial cells derived from new vessels.

The *deep parenchymatous keratitis* is always secondary to anterior uveitis, the infection spreading from the ciliary body and along the deep episcleral vessels. It differs from ordinary interstitial keratitis in that it does not clear up, but permanent discoloration remains.

Lepromata, or granulation-tissue tumours, are caused by infection spreading from the episclera, so that they originate in the limbus. A crescentic opacity appears at the periphery of the cornea and spreads towards the centre, and upon this nodules develop, which may cover the whole cornea (Babès). The growth is chiefly outwards, but the depth of infiltration varies much. In the episclera the fixed tissue-cells proliferate moderately (Lie), and the nodules are surrounded by large thin-walled vessels. Meyer and Berger describe a leproma in which there were many large epithelioid and spindle-shaped cells lying in a reticulum, so that it resembled a sarcoma. The granulation tissue contains round and spindle-shaped clumps of bacilli. The surface may ulcerate, but usually the epithelium is very resistant in all three types, and may proliferate downwards, forming epithelial plugs.

A similar case has been reported by Chiarini and Fortunati.

The substantia propria also offers considerable resistance to infiltration, but it may be ultimately entirely destroyed, Descemet's membrane alone remaining intact. Bowman's membrane easily succumbs, the epithelium lying on a thin layer of connective tissue.

Franke and Delbanco's cases were of the maculo-anæsthetic type, but showed similar histological features.

NEISSER.—Virchow's Archiv, ciii, 1886. MEYER AND BERGER.—A. f. O., xxxiv, 4, 1888. POLLOCK.—Leprosy as a Cause of Blindness, London, 1889. PHILIPPSON.—B. z. A.,

xi, 1893. CHIARINI AND FORTUNATI.—Ann. di Ott., xxiii, 1894. WINTERSTEINER.—Wiener klin. Woch., 1895. DOUTRELEPONT AND WOLTERS.—Arch. f. Derm., 1896. BABÈS.—Untersuchungen u. den Leprabacillus, etc., 1898. * BORTHEN AND LIE.—Die Lepra des Auges, Leipzig, 1899. FRANKE AND DELBANCO.—A. f. O., l, 2, 1900. ULENHUTH AND WESTPHAL.—Klin. Jahrbuch, Jena, 1900. NEVE.—Brit. Med. Jl., 1900.

SUPERFICIAL PUNCTATE KERATITIS

Superficial punctate keratitis was first described by Fuchs (1889), later by Stellwag v. Carion, Reuss (*keratitis maculosa*), Adler (*keratitis subepithelialis*), and others. Unlike reticular and nodular opacities (q. v.) the disease commences with inflammatory symptoms, and resembles herpes febrilis. Minute grey spots occur at once or after an interval of days or weeks. They vary from ten to twenty to over a hundred, and are often in rows or groups, generally in the central part of the cornea. They are quite superficial, and the epithelium is raised by them.

Nuel has examined corneal fragments microscopically. He found dense networks of fibres, staining deeply with alum carmin, in the substantia propria beneath Bowman's membrane. The lamellæ were œdematous and homogeneous, and the lymph-spaces were dilated. The filaments were between the lamellæ, and were apparently connected with the corneal corpuscles. They were massed under Bowman's membrane and diminished in number deeper in the cornea. The epithelium was œdematous, and showed degenerative changes; at the spots there were often cystic spaces containing granular material. Occasionally Bowman's membrane was destroyed and replaced by a network of fibres. Nuel regards the filaments as fibrin undergoing hyaline degeneration. In similar pathological conditions—though differing clinically—he has found aggregations of cocci.

Herbert states that a form of superficial punctate keratitis is common in Bombay. He was able to isolate an encapsuled bacillus from the epithelial scrapings. The capsules are 3·2 μ long by 1·6 μ broad; the bacillus stains feebly, and is decolourised by Gram.

FUCHS.—Wien. klin. Woch., 1889. STELLWAG V. CARION.—Wien. klin. Woch., 1889. REUSS.—Wien. klin. Woch., 1889. ADLER.—C. f. A., xiii, 1889. MARCUS GUNN.—T. O. S., x, 1890. BRONNER.—T. O. S., xii, 1892. NUEL.—A. d'O., xiv, 1894; xvi, 1896. HERBERT.—Ophth. Rev., xx, 1901.

SCLEROSING KERATITIS

In scleritis if a nodule is situated near the margin of the cornea an opacity develops in the deeper layers of the latter. It is triangular, with the apex towards the centre of the cornea. Other spots may also develop in the cornea. The thinner apex of the opacity may clear up, but the base remains permanently and becomes bluish white like the sclerotic; hence the term sclerosing keratitis (v. Graefe). With recurrent attacks of scleritis the opacity gradually advances, and may invade the whole cornea except a small central area.

Microscopically in severe scleritis the substantia propria of the cornea becomes infiltrated at the periphery (*see* Fuchs' 'Text-book,'

fig. 64). Vascularisation takes place, with the deposition of fibrous tissue, which renders the cornea opaque.

Purulent Keratitis

The intact epithelium offers an insurmountable obstacle to the invasion of the cornea by almost every organism which occurs in the conjunctival sac. A notable exception is the gonococcus, which is able successfully to attack the normal epithelium, disintegrate it, and invade the substantia propria. The diphtheria bacillus can probably act in the same manner, but in each case it is necessary for the organisms to remain undisturbed in contact with the epithelium for a considerable time. There are, however, many conditions which assist the entry of bacteria. Minute abrasions from foreign bodies, etc., are common, and the denuded surface offers little resistance to invasion. In other cases the resistance of the epithelium itself is diminished or abrogated by drying, as in xerotic conditions, or by actual necrosis due to deficient nutrition, as in keratomalacia. Further, œdema may lead to desquamation, or desquamation of the entire surface may be due to neuro-paralytic keratitis.

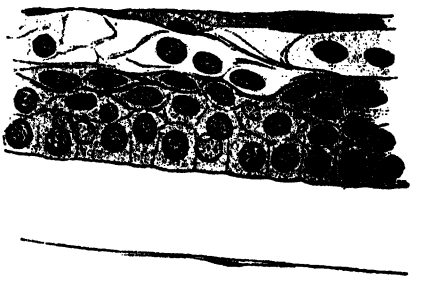


Fig. 127.—Action of Cocain on the Epithelium.

Fuchs, T. O. S., xxii. Prolonged action of cocain before enucleation. Note the swelling and œdema of one of the superficial layers.

A more minute examination of the epithelium in these various conditions will readily prove the weakening of this, the first line of defence. We have already examined the state of the epithelium in œdema and the desquamation resulting from it (*v.* p. 175). An analogous condition is found after prolonged instillation of cocain, especially if the lids are not closed in the intervals. The epithelium becomes opaque and dull, and is finally thrown off. The superficial layers swell (Fig. 127) and become loosened (Fig. 128). They are then detached, and a remarkable change takes place in the basal cells (Fig. 129), groups

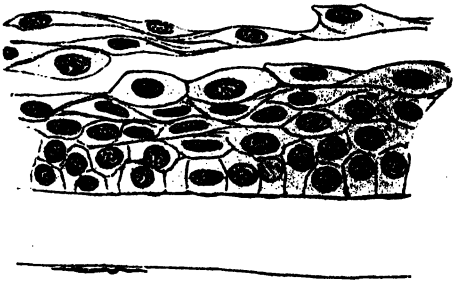


Fig. 128.—Action of Cocain on the Epithelium.

Fuchs, T. O. S., xxii. Exfoliation of superficial layers of epithelium.

of which become changed into a light mass with shrunken nuclei scattered here and there. In consequence of the alteration of the basement layer,

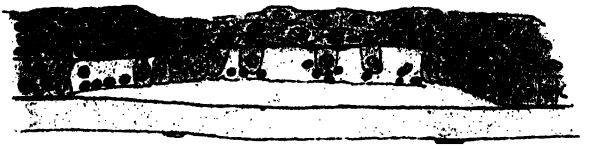


FIG. 129.—ACTION OF COCAIN ON THE EPITHELIUM.

Fuchs, T. O. S., xxii. Desquamation of the superficial layers. Degeneration and coalescence of groups of basal cells, leaving free nuclei. This would eventuate in total desquamation and the formation of abrasions.

the whole epithelium becomes detached from Bowman's membrane, and may be exfoliated.

The epithelium may undergo degenerative changes from various other causes, resulting in partial or complete atrophy (*v.* p. 225).

Enough has been said to show the extreme importance of the epithelium as a protective mechanism, and also the multitudinous ways in which its vitality may be affected. Further, the nature and extent of the affection varies with conditions, both local and general. Added to

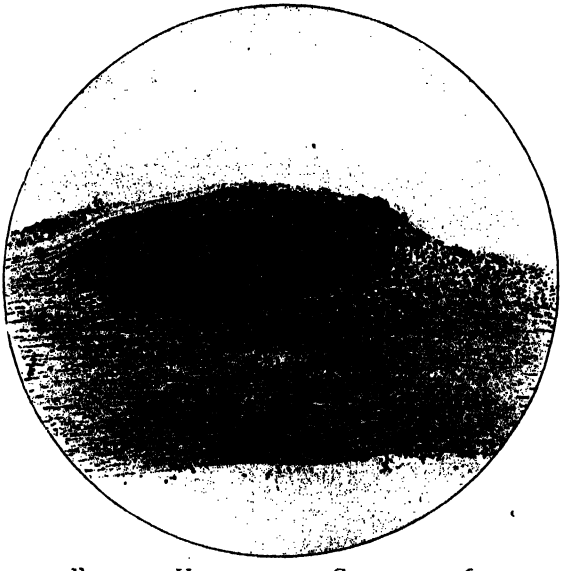


FIG. 130.—ULCER OF THE CORNEA. × 60.

Infiltrated edge of an hypopyon ulcer. Note the swelling from œdema and infiltration. Bowman's membrane is continued unchanged for a considerable distance beyond the epithelium.

these factors is the variety of the agents of attack, the nature of the resultant ulceration differing with the organism. The relative parts

played by all these factors have been accurately apportioned in very few cases. In badly nourished corneæ ulceration is apt to be deep, leading to early perforation, and also extensive, resulting in wide-spread necrosis. Such septic ulcers, due to the attack of ordinary pyogenic organisms,



FIG. 131.—ULCER OF CORNEA.

Fuchs, T. O. S., xxii. Ingrowth of epithelium between the lamellæ of the cornea at the edge of an ulcer. The epithelial cells are intermingled with leucocytes, which also invade Bowman's membrane.

occur after injuries in asthenic conditions in keratomalacia, lagophthalmos, keratitis neuro-paralytica, etc.

In the commonest form of suppurative keratitis—the corneal ulcer—there is a localised necrosis in the most anterior layers of the cornea. The sequestrum is partly disintegrated and cast off into the conjunctival sac, and partly adheres to the surface of the ulcer. Usually the epi-

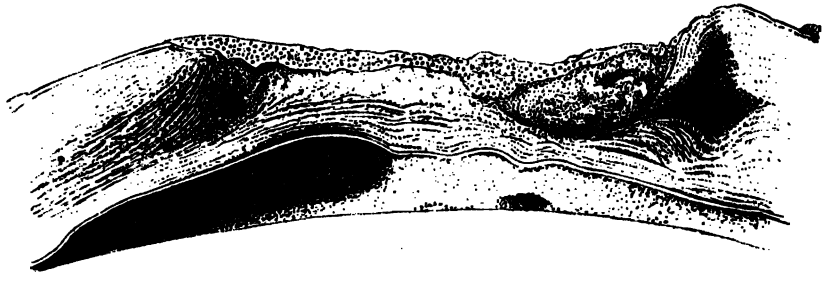


FIG. 132.—ULCER OF CORNEA.

Fuchs, T. O. S., xxii. Epithelium growing over pus and necrotic tissue, which cover the floor of the ulcer.

thelium is destroyed and cast off over an area considerably larger than the ulcer itself, and the same applies to Bowman's membrane, though this is not always destroyed so extensively (Fig. 130). The epithelium, however, rapidly advances towards the ulcer, grows over its edge, and

even penetrates, sometimes deeply, between the separated lamellæ, the epithelial cells often mingling intimately with the pus-corpuscles (Fig. 131). Not only so, but it may grow over the slough and purulent lymph which covers the floor of the ulcer or perforation, and may even form regular cylindrical basement cells reposing upon purulent matter (Fuchs) (Fig. 132). Similarly it will grow over blood-clot which may be present. When the final line of demarcation is determined and the dead material is completely cast off, this epithelium will of course suffer a like fate. In the *progressive* stages the ends of the broken lamellæ are swollen by œdema, and are separated by masses of pus-cells, which also infiltrate the lymph-spaces for a considerable distance around and beneath the ulcer. The margins of the ulcer therefore usually project considerably above the surface of the cornea (Fig. 133). This infiltrated area appears as a grey zone around the ulcer (*v.* p. 187). When the dead material has been thrown off the ulcer is somewhat larger, but the cloudiness has disappeared, the base and edges are smooth and transparent, and the *regressive* stage is reached. Meanwhile vascularisation has been going on, and cicatrisation now commences. This occurs in



FIG. 133.—MARGIN OF A CORNEAL ULCER.
Fuchs, T. O. S., xxii. Swelling of the edge by imbibition of fluid.

exactly the same manner as in the healing of corneal wounds, the processes gone through by the epithelium and the granulation tissue being identical (*v.* p. 151). The regenerative changes are ill-marked in cases of general asthenia, *e. g.* in keratomalacia (Sachsalber).

In all cases of acute keratitis, irritant substances diffuse from the cornea into the anterior chamber, and there act upon the blood-vessels of the iris and ciliary body. The result varies in degree, but the change in character of the aqueous is often very marked. From being a fluid which contains only 0·12 per cent. of proteid material, it becomes highly albuminous, owing to the injury inflicted upon the walls of the uveal vessels. Leucocytes are also present, and a fibrinous coagulum may be formed upon the posterior surface of the cornea and often upon the anterior surface of the iris. When the action of the toxins is more intense the number of leucocytes is enormously increased, and the aqueous becomes cloudy. These subsequently sink to the bottom of the anterior chamber and form an hypopyon. The typical *hypopyon ulcer* has certain specific characters, which will be discussed separately. It need only here be emphasised that the hypopyon originates from the vessels of the iris and ciliary body, and not from the cornea; and that

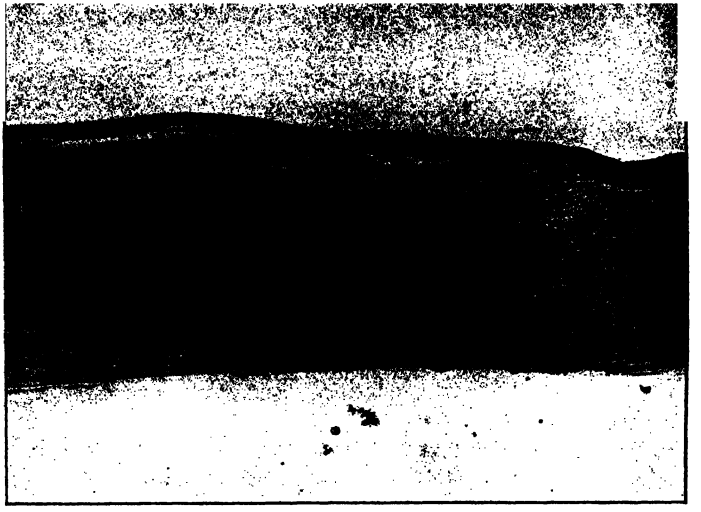


FIG. 134.—LEUCOMA OF CORNEA. × 60.

Scar following ulceration. Note the "levelling tendency" of the epithelium; the fibrillation and extensive destruction of Bowman's membrane; the irregularity of the scar tissue as compared with the deeper intact lamellæ; the infiltration and vascularisation of the substantia propria.

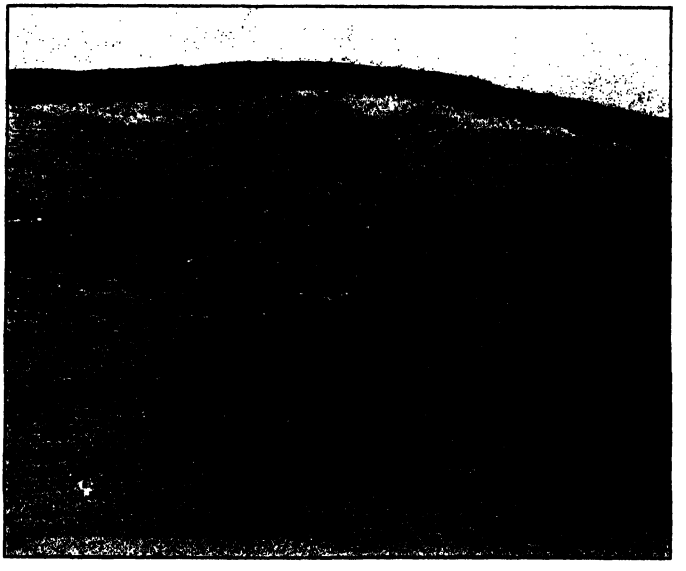


FIG. 135.—LEUCOMA OF CORNEA. × 60.

Scar two months after abrasion, which was followed by ulceration. The epithelium is ill-formed; Bowman's membrane is broken up and displaced. The substantia propria shows interstitial infiltration and vascularisation, almost limited to the superficial layers (*cf.* True Interstitial Keratitis, Fig. 123).

it is therefore sterile. This accounts for the rapidity with which it is frequently reabsorbed, and also for its being, unlike pus in general, relatively innocuous. The hypopyon varies greatly in consistence, being usually very fluid, but occasionally forming a dense fibrinous coagulum. The latter occurs in more severe cases, and is less readily absorbed.

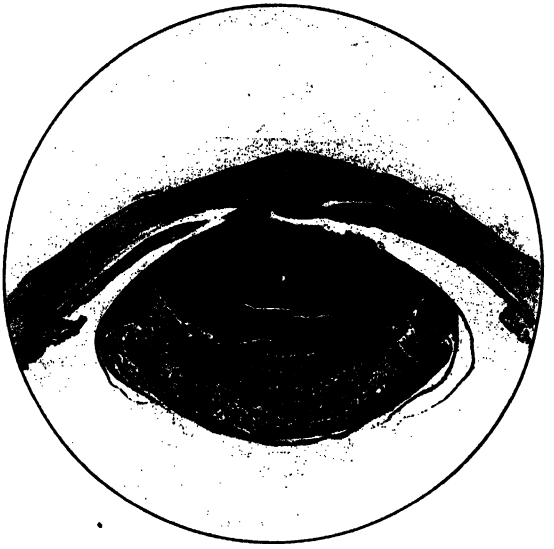


FIG. 136.—ULCER OF CORNEA. × 6.

Adhesion of lens to cornea after an injury, followed by hypopyon ulcer. The centre of the cornea is replaced by vascular scar tissue, which extends backwards to the iris and lens. The lens capsule is ruptured, and the anterior part of the cortex is infiltrated with leucocytes.

Absorption takes place principally through the meshes of the ligamentum pectinatum iridis.

SACHSALBER.—Z. f. A., ix, Ergänzungsheft, 1903.

HYPOPYON ULCER

The typical hypopyon ulcer, or *ulcus serpens* (Saemisch), is a greyish-white or yellow disc, occupying nearly the centre of the cornea. The opacity is greater at the edges than the centre, and is generally well marked in one special direction. Grey striæ extend from the margin of the disc into the transparent cornea. There is severe iritis, with posterior synechiæ, and hypopyon.

The association of hypopyon with inflammation of the cornea was called *hypopyon keratitis* by Roser in 1856. Saemisch recognised the characteristic tendency of the typical hypopyon ulcer to affect the superficial layers of the cornea and to spread over the surface; he therefore called it ulcus serpens (1870). Illustrations of the condition appeared in the atlases of Pagenstecher and Genth (1875) and Wedl

and Bock (1886). The first minute anatomical description was published by Verdese (1887), and it is interesting, in the light of recent polemics, to note that he describes perforation of Descemet's membrane without complete perforation of the whole cornea. Experimental investigations were carried out by Verdese (1889), Silvestri (1891), Leber (1891), and cases were described by Wagenmann (1892), Marple (1893), Fuchs (1893), Nuel (1895). In 1896 a very important series of observations was published by Uhthoff and Axenfeld, comprising five cases of ulcus serpens, four of keratomalacia, three of commencing panopthalmitis, and one of mycotic keratitis. More recent papers by Wagenmann, Green and Ewing, Elschnig, Druault and Petit, E. v. Hippel, Levy,

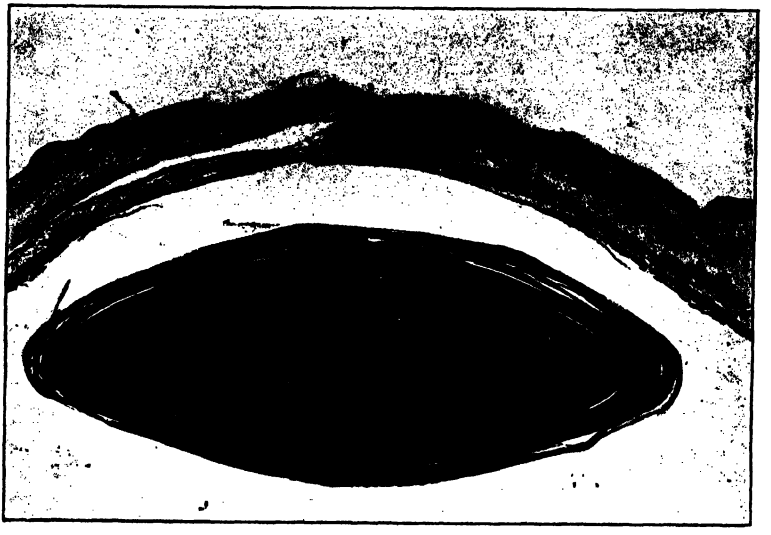


FIG. 137.—HYPOPYON ULCER. × 10·5.

There is very extensive ulceration of the cornea, the floor of the ulcer consisting only of Descemet's membrane and a few densely infiltrated lamellæ The lower half of the a. c. is full of pus; the more faintly stained part is chiefly fibrin; the lower angle contains blood. The iris is intensely inflamed. On the anterior surface of the lens is a pigmented tag, the remnants of a posterior synechia which has torn away.

Wintersteiner, and others, deal principally with details, some of which cannot yet be said to be finally settled.

According to Fuchs, the earliest stage of ulcus serpens is a dense infiltration of the superficial lamellæ in about the centre of the cornea. The lamellæ over the infiltrate swell up and exfoliate, so that a flat open ulcer is formed, the floor of which consists of fibres which have been heaved up, and are swollen into an almost homogeneous mass, amongst which are sparsely scattered pus-corpuscles. It is only at the margins of the ulcer that the remains of the infiltrate can be distinguished, and here it penetrates—appearing in cross section like a wedge—into that portion of the cornea which is still sound. This corresponds with the

yellow advancing border; it keeps insinuating itself farther and farther between the lamellæ, so as at first to lift them up and then detach the superficial layers. Often the ulcer advances in one direction only. The progressive portion then looks like a yellow crescent. At other parts the wedge-shaped infiltrate is absent, and the epithelium extends over the edge of the ulcer and on to its floor. This part, however, is not necessarily healed, and the epithelium may lie on dying tissue or *débris*. The lamellæ here, indeed, are often swollen and hyaline, and contain no stained corpuscles; consequently they are probably necrotic. The same applies in less degree to many of the deeper lamellæ.

Bowman's membrane is destroyed over the ulcer, and is often split up for a considerable distance beyond. In some cases the lamellæ near



FIG. 138.—ULCER OF CORNEA. × 22.

Edge of hypopyon ulcer; to the left is a paracentesis wound, over the edges of which epithelium is growing. The inner part of the wound is filled with leucocytes. The cornea is densely infiltrated with polymorphonuclear leucocytes, which also cover the iris and parts of the back of the cornea.

the ulcer are separated by fibrinous coagula (Uhthoff and Axenfeld). The infiltration around the ulcer is usually fairly uniform in all the cases which have been examined, extending without break to the periphery of the cornea; *i.e.*, Leber's (central) infiltration ring is usually absent in man. This is probably due to the toxins not being sufficiently strong to paralyse the leucocytes even in the immediate neighbourhood of the ulcer, a view which is supported by the fact that most cases are due to pneumococci (*v. infra*), whereas Hertel observed the infiltration ring in cases of streptococcic ulcer.

The middle layers of the cornea are least infiltrated. As Descemet's membrane is approached the infiltration increases rapidly, so that a definite *posterior infiltration*, or so-called posterior abscess, is formed.

This corresponds in situation with the site of the ulcer. Its origin is a subject of dispute. Two views are open, viz., that the leucocytes are derived from the peripheral vessels, and travel inwards (Wintersteiner); or that they are derived from the hypopyon, and travel forwards (Elschnig). Now it is a well-established fact that leucocytes do not pass through an intact Descemet's membrane; hence the condition of Descemet's membrane is of prime importance for the solution of the problem. There is no doubt that Descemet's membrane offers great resistance to inflammatory and other processes, so that it often remains unbroken when all the other layers of the cornea have been destroyed; keratocele, indeed, depends upon this fact. All observers agree that Descemet's membrane is frequently split into layers, which are separated



FIG. 139.—ULCER OF CORNEA. × 11.

Section across the edge of an hypopyon ulcer. The ulcer is healing and is covered with irregular epithelium. The floor and edges are vascularised. The posterior lamellæ of the cornea are intact and only slightly infiltrated. The base of the ulcer is formed by a thick layer of scar tissue. Nearer the centre of the ulcer there was an anterior synechia.

by aggregations of leucocytes, and also that it may be ultimately broken through (Fig. 140). Wintersteiner thinks that this takes place from before backwards. Elschnig and his followers hold that *early perforation (Frühperforation) of Descemet's membrane* is a conspicuous feature of ulcus serpens, and that it is due to attack from behind. They support this idea by cases in which the opening in the posterior layers of the split membrane is greater than that in the anterior layers. This condition is also described as an *internal ulcer*.

As already mentioned, Descemet's membrane was perforated in Verdese's case. This and other cases are attributed by Petit to folds, which often look like perforations in sections. Wagenmann, E. v.

Hippel, and Druault and Petit found deep ulceration with normal Descemet's membrane; Uhthoff and Axenfeld, Green and Ewing found early perforation. Green and Ewing, indeed, support the exploded view that the leucocytes of the hypopyon are derived from the cornea. It is an important fact that most of the cases with perforation of Descemet's membrane were glaucomatous eyes. Greeff brings forward the case of a child with fairly extensive hypopyon keratitis who died of pneumonia. There was a well-developed posterior infiltration with quite intact Descemet's membrane. He cites the sterility of hypopyon as an argument against Elschnig's view, but the ferment action of leucocytes is not due to organisms, though it may be stimulated by their presence.

Elschnig's theory is supported by Fuchs, but it can be scarcely said to be proved beyond cavil.

The endothelium is often absent over a large area, especially behind the ulcer, even when Descemet's membrane is intact. Uhthoff and Axenfeld found giant-cell-like masses of endothelium free in the hypopyon; in other places leucocytes separated the endothelium from the



FIG. 140.—ULCER OF THE CORNEA.

Fuchs, T. O. S., xxii. Swelling of the floor of the ulcer by imbibition of fluid. Splitting and destruction of Descemet's membrane by infiltration from behind ("early perforation"). Hypopyon.

membrane. The cells themselves showed pathological changes—vacuolation, faint nuclear staining, etc. Elsewhere there was proliferation and the formation of stellate cells. The leucocytes often adhere especially in the neighbourhood of the posterior infiltration, and are continuous with it when Descemet's membrane is perforated. When the membrane is split, the clefts are also filled with leucocytes.

The *hypopyon* was at first thought to be derived from the cornea (Horner); it is now almost universally believed to come from the vessels of the iris and ciliary body (Leber, Uhthoff and Axenfeld, Bach, Wagenmann, etc.). This view is supported by the presence of pigment granules in the hypopyon (Uhthoff and Axenfeld). The cause of the hypopyon is chemotaxis, and this accounts for the main aggregation of leucocytes being upon the back of the cornea, as near as possible to the site of infection; the iris is often covered by a fibrinous network, containing relatively few cells, so that possibly most of the leucocytes are derived from the ciliary body and ligamentum pectinatum (Nuel). Chemotaxis is due to the diffusion of toxins only, the hypopyon being sterile as long as Descemet's membrane is intact (Leber, Uhthoff and Axenfeld, Bach, etc.).

Bacteriology.—The credit of the discovery that the typical ulcus serpens is due to pneumococci rests with Uhthoff and Axenfeld (1896), and their results have been confirmed by investigators in all parts of the world. In fifty cases they found pneumococci only, twenty-six times; mixed with other organisms, seven times; other bacteria only, thirteen times; no bacteria, four times. It has been found impossible to reproduce the typical ulcus serpens in animals by inoculation. Neither does it occur in its typical form in children, in whom hypopyon ulcer runs a different and usually milder course.

The ulcus serpens may be regarded as the typical form of hypopyon ulcer; it is by no means the only form. *Atypical hypopyon ulcer* is usually due to other pyogenic organisms than the pneumococcus—staphylococci, streptococci, bacilli, etc., though none of these produces a specific type of ulcer. There is a greater tendency to rapidly invade the deeper layers of the cornea. Perforation occurs earlier, and the dangers of panophthalmitis are increased. Quite occasionally pneumococci are present, mixed with other organisms; and occasionally, too, pneumococcic infection assumes an atypical form (Uhthoff). In gonorrhœal and diphtherial infection the corneal processes are chiefly due to secondary infection by other pyogenic bacteria, the gonococci or diphtheria bacilli merely facilitating the entry of these by the action of their toxins. The same applies to the xerosis bacilli which are present in such large numbers in many xerotic conditions, keratomalacia, etc., though here the bacilli probably play an almost purely passive part. The most interesting form of atypical hypopyon keratitis is that produced by the *Aspergillus fumigatus*, which demands special consideration (*v. infra*).

Hertel has exhaustively investigated nineteen cases of suppurative keratitis; eleven were cases of ulcus serpens, the remainder infected phlyctenular ulcers, etc. In ten cases, including six of ulcus serpens, the pneumococcus was the cause in eight, being mixed with staphylococci in one; the remaining two were due to streptococci. The form and size of the ulcer naturally varied with the duration; it was at first flat, the advancing edge being often raised. It became deeper after long duration, but here too the progress on the surface was greater than in depth. The size also varied with the virulence of the bacteria; in two cases, due to pneumococci, it was extensive after three days' duration, and in one of these the cocci killed a mouse in sixteen hours. The ulcer was also greater in glaucomatous eyes than in others, the duration being the same.

The epithelial defect was in many cases much more extensive than the ulcer. Besides very active proliferation of epithelium in long-standing cases (Uhthoff and Axenfeld), Hertel also found it in the acute stage. Mitoses were commoner near the limbus than at the edge of the wound.

Bowman's membrane was occasionally more extensively destroyed than the lamellæ; the edge was broken up into fibrillæ. The substantia propria showed infiltration and necrosis, the latter indicated by bad staining reaction. The necrotic areas showed the presence of cocci. In the reshest cases these were present in the superficial layers; in others

they formed spindle-shaped masses in the undermined edges of the ulcer, being posterior to the infiltration. In an early perforated wound the cocci lay in large numbers in the necrotic lamellæ directly upon Descemet's membrane. They were not seen in the epithelium, as found by Wagenmann. The reaction zone in fresh cases was at a little distance around the masses of cocci. In the slighter cases a line of demarcation was formed in the zone of infiltration. In the more severe, fresh necrosis and infiltration occurred, and here the cocci might be embedded in round-cells, some being intra-cellular. The streptococcic cases went on rapidly to perforation, and, as already mentioned, Leber's infiltration ring was seen here.

At the edges of the necrotic areas degeneration of the corneal corpuscles was manifested. The cell-processes were short or absent, and the nuclei were degenerated. Necrosis of the lamellæ was shown by fine granulation and fibrillation. In the surrounding areas inflammatory spindles (*v.* p. 188) were present.

Hertel found "early perforation" of Descemet's membrane in five cases; it may occur as early as two and a half to three days after the commencement of ulceration. It appeared to be due to histolytic effect of the leucocytes; in two cases it was undoubtedly due to erosion from behind, since the posterior corneal infiltration was absent in the situation of the apertures. Hence posterior infiltration is not essential to the development of early perforation of Descemet's membrane. Hertel agrees with Elschnig and others that glaucoma is a weighty factor in causing early perforation; it was present in four cases out of six. It doubtless acts through defects of circulation and nutrition (Elschnig) as well as through mechanical means. That the latter—mere increase of tension—can lead to rupture of Descemet's membrane is well known (*v.* Fig. 108).

Hertel regards the iris as the main source of the hypopyon, in opposition to Uhthoff and Axenfeld; the changes in the angle and ciliary body were less marked. It contained intra- and extra-cellular pigment and endothelial cells; there were no cocci present.

Römer's experiments with antipneumococcic serum are of great interest.

ROSER.—A. f. O., ii, 2, 1856. SAEMISCH.—Das Ulcus serpens, Bonn, 1870. DINKLER.—A. f. O., xxxiv, 3, 1888. VERDESE.—A. d'O., vii, 1887; ix, 1889. SILVESTRI.—A. f. O., xxxvii, 2, 1891. LEBER.—Die Entstehung der Entzündung, Leipzig, 1891. WAGENMANN.—A. f. O., xxxviii, 3, 1892. MARPLE.—A. of O., xxii, 1893. GASPARRINI.—Ann. di Ott., xxii, 1893. FUCHS.—Text-book. BASSO.—Internat. Congress, Rome, 1894. NUEL.—A. d'O., xv, 1895. SECONDI.—Clinica moderna, 1895. * UHTHOFF AND AXENFELD.—A. f. O., xlii, 1, 1896; xliv, 1, 1897. BACH AND NEUMANN.—A. f. A., xxxiv, 1897. GREEN AND EWING.—T. Amer. O. S., 1896, 1898. ELSCHNIG.—A. f. O., xlv, 1898. E. v. HIPPEL.—A. f. O., xlvii, 1898. DRUAULT AND PETIT.—A. d'O., xix, 1899. LUNDSGAARD.—K. M. f. A., xxxviii, 1900. PETIT.—K. M. f. A., xxxix, 1901. ELSCHNIG.—K. M. f. A., xxxix, 1901. LEVY.—K. M. f. A., xxxix, 1901. WINTERSTEINER.—A. f. O., lii, 3, 1901. ELSCHNIG.—A. f. O., liii, 2, 1901. DÖTSCH.—A. f. O., xlix, 2, 1900. * HERTEL.—A. f. O., liii, 2, 1901. RÖMER.—A. f. O., liv, 1, 1902. KRÜGER.—Z. f. A., x, 1903.

Mycotic Keratitis

Keratomycosis aspergillina (Schimmelpilzkeratitis) affords a characteristic clinical picture. The central part of the cornea shows an infiltration, which later undergoes superficial disintegration, and is distinguished by its dry, crumbling surface. A grey or yellow line of demarcation forms about this area, gradually deepening into a gutter, and ultimately leading to the exfoliation of the enclosed portion of cornea, which in the meantime has become necrotic. Hypopyon is present, but the irritative symptoms are slight, the whole course being very chronic.

The first case was published by Leber in 1879; it resulted from the husk of an oat grain flying into the eye. The second case was published by Berliner (1882) and investigated later by Uhthoff; it followed a blow by a pear. In the third case, described by Fuchs, the man was

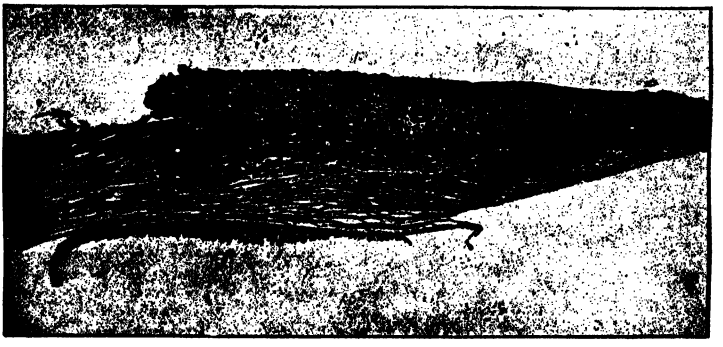


Fig. 141.—Mycotic Keratitis. × 20.

From a photograph by Buchanan. Meridional section of cornea, showing area of slough penetrated by the fungus, zone of inflammatory infiltration surrounding the slough, and the margin of the ulcerated surface from which the slough has been separated.

a miller; he had an attack of herpes corneæ febrilis, and was probably infected by the flour at the time when the corneal epithelium was abraded. Other cases have been reported by Uhthoff and Axenfeld, Schirmer, Nobbe, Wicherkiewicz, etc. In Nobbe's case there was a perforating wound with a knife. The eye was excised owing to sympathetic ophthalmia, and the fungus was found in the vitreous (*cf.* Römer).

The disease is due to a mould, the *Aspergillus fumigatus*, and is especially characterised by the tendency to the formation of a sequestrum (Fig. 141). This sequestrum is found to be permeated by the mycelium, which forms a rich network of fibrils, showing dichotomous division (Fig. 142). Fructification is absent in the cornea, probably because the cornea is below the optimum temperature for growth. The fibres stain well with hæmatoxylin, better with Löffler's methylene blue and Weigert's fibrin stain, not at all with carmin; they are 3 to

4 μ broad (Schirmer). The condition is easily reproduced in rabbits by inoculation of the cornea (Leber, Uhthoff and Axenfeld). Colonies can be obtained upon blood-serum, not upon glycerin agar or bouillon (Uhthoff and Axenfeld). Gentilini obtained profuse cultures upon glycerin agar, as well as upon potato and bread. They were greenish in colour, and showed under the microscope a richly branching mycelium with many fructifications. These were club-shaped on a fairly long stalk, the conidia themselves being round. *Aspergillus fumigatus* is the only species which has been observed in the cornea; other pathogenic species (*A. flavescens, niger, mucor,* etc.) have not been found,



FIG. 142.—MYCOTIC KERATITIS. × 250.

From a photograph by Buchanan. Meridional section through the sloughing area, showing the mycelium of the fungus as a densely felted network. The anterior layer is composed entirely of mycelium (not of epithelium), and Bowman's membrane is destroyed.

though many produce mycotic keratitis when inoculated into rabbits' corneæ (Leber).

Schirmer and Nobbe were able to examine the whole eyes. In Schirmer's case there was an old leucoma adhærens. Much of the cornea was ulcerated; in the middle of the ulcer the whole cornea was pervaded by the mycelium of the fungus. This also spread back along an anterior synechia into the anterior part of the vitreous. For a large area around the network in the cornea there were no nuclei stained, so that the tissue was necrotic. Beyond this was a zone of dense round-celled infiltration, in every respect answering to Leber's infiltration ring, which is so rare in other types of hypopyon ulcer.

Keratomycosis aspergillina does not necessarily give rise to the

picture of hypopyon keratitis. In rare cases it produces a simple infiltration resembling fascicular keratitis (Uhthoff and Axenfeld, Kayser). There is usually, however, the same formation of a sequestrum in these cases.

LEBER.—A. f. O., xxv, 2, 1879. UHTHOFF.—A. f. O., xxix, 3, 1883. * LEBER.—Die Entstehung der Entzündung, Leipzig, 1891. FUCHS.—Wiener klin. Woch., 1894. UHTHOFF AND AXENFELD.—A. f. O., xlii, 1, 1896; xliv, 1897. SCHIRMER.—A. f. O., xlii, 1, 1896. NOBBE.—A. f. O., xlv, 3, 1898. GENTILINI.—B. z. A., xlv, 1900. WICHERKIEWICZ.—A. f. A., xl, 1901. RÖMER.—K. M. f. A., xl, 1902. * KAYSER, JOHNSON.—K. M. f. A., xli, 1903. BUCHANAN.—T. O. S., xxiii, 1903.

PERIPHERAL ANNULAR INFILTRATION

Besides the ring infiltration observed by Leber close to a central ulcer in rabbits, and very rarely seen in man, there is a peripheral ring

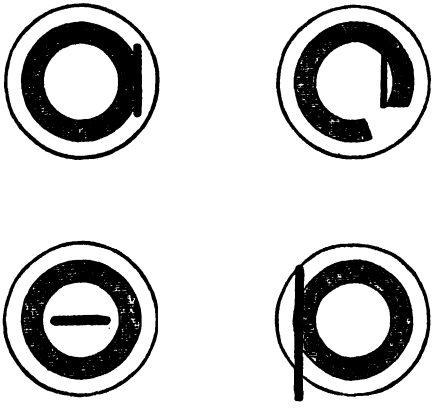


FIG. 143.—PERIPHERAL ANNULAR INFILTRATION OF THE CORNEA.
Treacher Collins, Ophth. Rev., xii. The thick line shows the position of the wound, the hatched ring that of the infiltration. The latter is constant in position, whilst the former varies.

infiltration, or so-called *ring abscess*, met with occasionally in perforating wounds. It has received little attention in the text-books, being only mentioned by Saemisch and Vossius.

The first anatomical examination was by Fuchs, of a case following linear extraction in a diabetic. Four cases were later described by Treacher Collins (Fig. 143), who considered the condition opposed to Leber's views upon ring infiltration. The peripheral infiltration is, however, of a totally different nature to the central ring described by Leber. One of Hertel's cases possibly belongs to this category, but the subject has received exhaustive investigation by Fuchs in a recent paper.

Peripheral annular infiltration occurs most commonly after small perforating wounds caused by chips of metal; it also occurs after operations, having been especially common in cataract extractions in the pre-antiseptic days, and very rarely after spontaneous perforation of

an ulcer, and in metastatic ophthalmitis. It appears usually very quickly after the injury; in four cases one day, five cases two days, three cases three days, two cases four days, one case eleven days (Fuchs); one case eight days (Treacher Collins). The ring is at first grey, then yellow;



FIG. 144.—PERIPHERAL SUPERFICIAL INFILTRATION OF THE CORNEA.
Fuchs, T. O. S., xxii. This type is comparatively innocuous, ending in absorption or the formation of a shallow ring ulcer.

1·5 mm. broad, with the peripheral edge 1—1·5 mm. from the limbus, though it may reach the limbus. The inner edge is less clearly defined than the outer. The edges of the wound are usually little infiltrated or not at all. The infiltration is invariably peripheral, irrespective of the position of the wound. The condition almost invariably goes on to panophthalmitis.

When infiltration of the wound occurs, it occupies the posterior



FIG. 145.—PERIPHERAL ANNULAR INFILTRATION OF THE CORNEA. × 7.
From a specimen sent by Prof. Fuchs.

layers and does not extend far peripherally. Aggregations of bacteria are always found between the lamellæ in the same situation.

The peripheral infiltration forms a ring concentric with the corneal margin, at first 1 to 1·5 mm. from it, but occasionally farther in older cases. It consists of two zones: (1) amongst the middle and superficial

lamellæ, (2) immediately in front of Descemet's membrane (Figs. 145, 146). The *anterior infiltration ring* is always most marked, the aggregation of leucocytes being often so great that the cornea is thickened, the surface projecting or even being folded. At the periphery of the ring the infiltration is greatest in the middle layers, the superficial layers being more affected as the centre of the cornea is approached. In some cases this is so marked that the anterior ring is itself divided into two zones, a superficial, more central one, and a peripheral deeper one. Various explanations may be given. The superficial leucocytes probably come from the peripheral loops of the corneal blood-vessels, the middle ones from the anterior ciliary vessels. Possibly the emigration is earlier from the limbus vessels, so that the leucocytes have wandered farther into the cornea; or emigration may be simultaneous, but the resistance of the lamellæ may be greater in the middle layers; or the deeper cells may tend towards the surface as they pass inwards (Fuchs). The last suggestion seems to be the least probable. Later, the infiltration is so

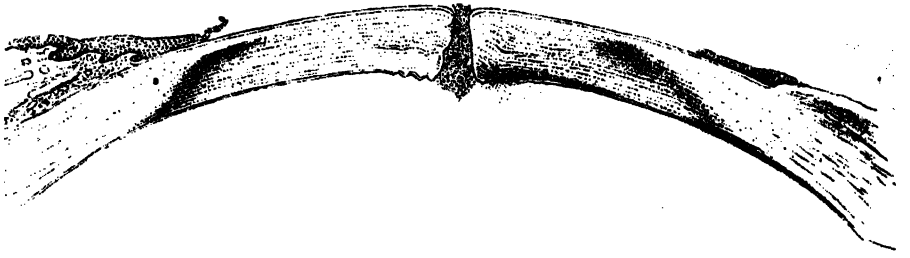


FIG. 146.—PERIPHERAL ANNULAR INFILTRATION OF THE CORNEA.
Fuchs, T. O. S., xxii; *see also* A. f. O., lvi.

intense in the superficial layers that necrosis occurs, Bowman's membrane is destroyed, and the swelling disappears, loss of substance replacing it.

The *posterior infiltration ring* is less constant; most of the cells lie directly upon Descemet's membrane, which is thus separated from the cornea. The anterior and posterior rings are usually separated by an area of diffuse infiltration. Descemet's membrane is intact in this situation, so that the leucocytes do not come from the anterior chamber, but wander in from the periphery. There is generally a wide clear zone between the infiltration and the periphery, but there is often a separate, very localised infiltration at the extreme periphery.

The corneal corpuscles are only stained well in the anterior layers; elsewhere they are pale or unstained. Regarding this as evidence of necrosis, the cornea is most necrosed in the deepest layers, and for a greater thickness near the centre; the necrosis never reaches the periphery.

The epithelium and endothelium are for the most part destroyed; Bowman's and Descemet's membranes mostly intact. The anterior chamber contains pus or fibrinous coagulum; elsewhere there is commencing panophthalmitis.

Bacteria were present in large numbers in the anterior chamber, and often in the vitreous; sometimes in the posterior layers at the edges of the wound. In the latter situation there was often no infiltration, absence of reaction being doubtless due to necrosis. Staphylococci and streptococci were each found twice; bacilli three times (twice in pure culture, once mixed with cocci).

Hanke, working under Fuchs, has recently described a specific bacillus; it was found in pure culture in the ulcer and in the hypopyon. The bacilli are long and thin, with rounded ends, 0·8—1·6 μ by 0·3 μ. They are mostly extra-cellular, stain deeply with the ordinary aniline dyes, but are negative to Gram. They are polymorphic in pure cultures, varying from short rods to whip-like filaments, 4 μ and more long; they show polar staining in old cultures. They do not form spores. They grow on all the usual culture media, producing a green fluorescence; they liquefy gelatine. They are facultative aërobes, and are motile in hanging drops. They are virulent for mice, causing death within 1—2 days when injected intravenously. Inoculated into guinea-pigs' or rabbits' corneæ they produce typical ring abscess.

Fuchs explains peripheral annular infiltration (ring abscess) of the cornea thus: Bacteria enter the eye, usually by a perforating wound, multiply within it, and set up purulent irido-cyclitis and a keratitis which attacks the cornea *from behind*. Ring infiltration follows by emigration of leucocytes from the peripheral vessels, and is directed towards the removal of the necrosed parts or sequestrum. Rarely this is successful, as in one of the cases reported; almost invariably it fails. This theory explains the situation of the necrosis in the cornea and the frequent absence of infiltration of the edges of the wound, which is never absent when bacteria attack the cornea from the surface. The condition is therefore quite different from Leber's central ring infiltration, the former being directed against a posterior sequestrum and the latter towards a superficial ulcer.



FIG. 147.—MARGINAL ULCER OF CORNEA.

Fuchs, T. O. S., xxii. Epithelium growing over the peripheral edge of a marginal ulcer, whilst the central edge remains bare and infiltrated with leucocytes.

SAEMISCH.—In G.-S., iv, p. 193, 1876. VOSSIUS.—Lehrbuch., 3rd ed., p. 391. TREACHER COLLINS.—Ophth. Rev., xii, 1893. HERTEL.—A. f. O., liii, 2, 1901. *FUCHS.—A. f. O., lvi, 1, 1903. HANKE.—Z. f. A., x, 1903.

MARGINAL ULCER

Various types of marginal ulcer of the cornea have been described (Fig. 147). zur Nedden divides them into two groups: (1) secondary to phlyctenular conjunctivitis and blennorrhœa of the conjunctiva; (2) primary and independent of conjunctivitis. The second group ncludes (*a*) Schmidt-Rimpler's furrow keratitis (*v. infra*), and perhaps Fuchs' marginal ulcer associated with the uric-acid diathesis, and

(*b*) those due to a specific organism isolated by zur Nedden. Two types of ulcer are due to this cause: (*α*) an isolated oval, sickle- or horse-shoe-shaped, or ring ulcer; (*β*) multiple punctate ulcers, with severe secondary conjunctivitis. The primary marginal affections may be associated with hypopyon.

The bacillus is straight or slightly curved, 0·9 *μ* long by 0·6 *μ* broad, with rounded ends; it is not stained by Gram. Two often lie end on, like diplobacilli. Diagnosis from the Morax-Axenfeld diplobacillus, etc., is only certain by cultural methods (*v.* p. 47).

ZUR NEDDEN.—A. f. O., liv, 1, 1902.

ATHEROMATOUS ULCER

Atheromatous ulcer (Fuchs), or *sequestrating scar-keratitis* (Wintersteiner), occurs in old leucomata and anterior staphylomata.

The scars in which these ulcers occur are nearly always the result of extensive destruction of the cornea with perforation. They consist of remnants of the cornea—fragments of Bowman's and Descemet's



FIG. 148.—ATHEROMATOUS ULCER OF CORNEA.

Fuchs, T. O. S., xxii; *see also* A. f. O., liii. Downgrowth of epithelium beneath calcareous plate in an old leucoma. The epithelium in front of the plate is necrotic.

membrane,—and of entangled iris—retinal pigment and fibres of the sphincter,—bound together by new connective tissue. In the early stage they are rich in vessels; these ultimately disappear, and calcareous particles are deposited in a tissue devoid of nuclei. The vitality of the scar is reduced to a minimum, so that stagnation occurs. The deposits are at first hyaline, and are found chiefly upon the surface, even in the epithelium; they grow by accretion, and gradually become impregnated with calcium salts. There is at first a peripheral zone of fine particles; later the calcareous masses are sharply limited. A narrow free space next appears between the mass and the rest of the scar.

The nature of the epithelium is influenced by the condition of the scar. If the latter is highly vascular, the epithelium is thicker than normal; it is flat on the surface, but fills all the inequalities of the scar, so that it assumes a papillary form. Cords of epithelium grow down into small and large clefts, and invade the gutter around the calcareous plates, which they also undermine, leading at last to the formation of a hard sequestrum (Fig. 148).

The whole surface is often succulent and rich in vessels, like pannus,

covered by thickened epithelium. This condition, however, is confined in many cases to the edges or to islands, the main part consisting of dense sclerotic tissue. Here the epithelium undergoes atrophy, with regressive changes, such as cornification and the formation of intercellular spaces. There are four ways in which the epithelium is removed: (1) simple atrophy and disappearance, owing to lack of nourishment; (2) cornification; (3) separation of the cells by fluid and the formation of cyst-like spaces; (4) heaving up of the epithelium—the so-called vesicular and bullous keratitis.

The growth of the epithelium under the calcareous plates helps the invasion of the tissues by bacteria, so that inflammation ensues, accompanied by extensive necrosis throughout the whole thickness of the scar. The infiltration around the mass is at first in two layers, an anterior and a posterior, which are separated by a layer in which the necrotic area is in continuity with the periphery. It differs therefore from an ordinary ulcer; the anterior infiltration is probably directed against the invading organisms, whilst the posterior is of the nature of a demarcating infiltration directed against the necrotic tissue. Gradually they meet, and the sequestrum is thrown off. It consists of compact fibrous tissue, devoid of stained nuclei, together with pus-cells; it may or may not contain calcareous material. The infiltration around the necrotic patch is cruciform in section, as in ulcus serpens. It differs from this, however, in not progressing towards the periphery. Clinically ulcus serpens travels quickly over the surface and gradually deepens, whilst the atheromatous ulcer scarcely enlarges at all on the surface, but rapidly deepens, and very often leads to panophthalmitis.

In mild cases there is merely necrosis and elimination of a superficial, calcified, or otherwise badly nourished layer. In severe cases the suppuration goes deeper, and invades the ciliary body; vitreous, etc., by way of the adherent iris, exactly as in cases of *late infection* described by Leber and Wagenmann.

Sections stained by Gram's method show clumps of cocci in the purulent infiltration, especially at the apex of the wedge, less on the surface.

Atheromatous ulcer is characterised, therefore, by necrosis followed by infiltration, thus differing from ordinary ulceration, in which these processes occur in the reverse order. It is further allied to rare cases of necrosis *en masse* of the cornea, such as have been described by Fuchs and Elschnig.

ARLT.—Lehrbuch. FUCHS.—A. f. O., liii, 1, 1901. DOLGANOFF AND SOKOLOFF.—A. f. A., xlvii, 1903. NECROSIS EN MASSE:—FUCHS.—K. M. f. A., xviii, 1880. ELSCHNIG.—Wiener med. Woch., 1899.

MOOREN'S ULCER

The so-called "rodent ulcer" of the cornea, first isolated by Mooren (1867), is a *chronic serpiginous ulcer* (Nettleship), which develops from the margin of the cornea and very slowly invades other parts of that structure, until finally the whole cornea may have become involved. The advancing edge is characteristically under-

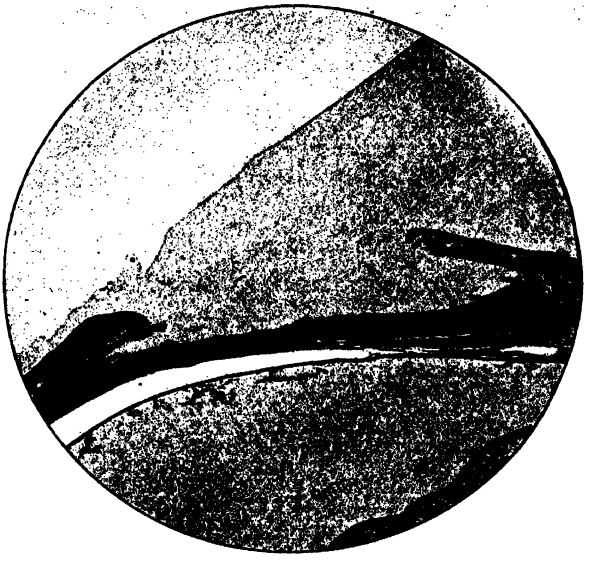


FIG. 149.—MOOREN'S ULCER. × 15.
From Lister, R. L. O. H. Rep., xv. Showing the whole ulcer.

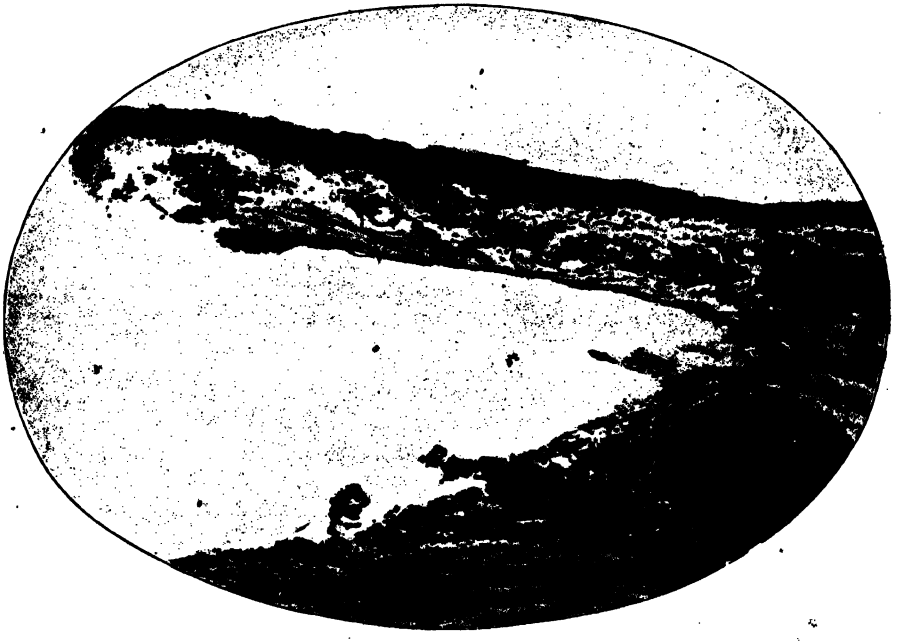


FIG. 150.—MOOREN'S ULCER. × 80.
From Lister. The overhanging edge of the ulcer. The epithelium is very irregular in thickness, and extends round the tip; the sub-epithelial tissue is infiltrated and vascularised. The floor of the ulcer is covered with broken down corneal tissue. On the right a round mass of epithelium is seen.

mined, as shown by its grey, cloudy appearance, and the fact that it can be lifted up. The ulcer often heals for a time, but sooner or later the symptoms of irritation recur, and the ulcer pushes its way somewhat farther into the cornea. The healed part is deprived of its superficial layers and remains cloudy; perforation never occurs.

Microscopical examinations have been made by Lawford (1889), Krey (1890), Hillemanns, Schmidt-Rimpler, and Lister. Lawford's case was regarded at the time as an ulcerating epithelioma. The posterior layers of the cornea were fairly normal, showing merely some increased nucleation, and in the peripheral part a few new vessels. Bowman's membrane was intact only over a small area, probably corresponding with an island which had not ulcerated. The floor of the ulcer consisted almost entirely of small round cells—a sort of

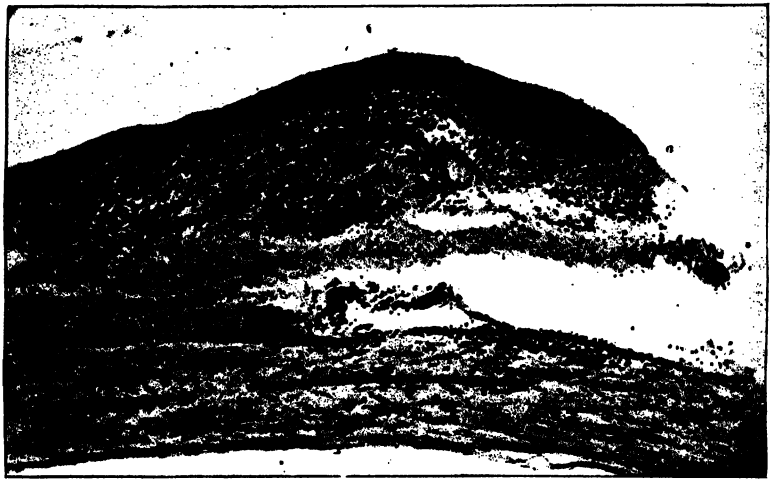


FIG. 151.—MOOREN'S ULCER. × 80.

From Lister. The outer edge of the ulcer, showing great infiltration with und-cells.

granulation tissue; here and immediately subjacent were numerous small blood-vessels.

The ulcer usually destroys about one third of the thickness of the cornea. The granulation tissue which is seen forming the floor of the active ulcer is thicker and more organised in the healed part. Here the total thickness of the cornea may exceed the normal. It is covered by much thickened epithelium, which has a very irregular base line, downgrowths often passing in various directions. Beneath this is the scar tissue, which is highly vascular and infiltrated with lymphocytes in the earlier stages, and consists of clear, fine fibrillæ in the older. This layer diminishes in thickness from the limbus towards the ulcer. Beneath it are the corneal lamellæ; Descemet's membrane and the endothelium are normal. At the periphery Hillemanns found some branches of the anterior ciliary arteries containing hyaline thrombi.

The overhanging edge at the advancing border of the ulcer usually consists not only of epithelium, but also of a varying number of corneal lamellæ, usually about one third the thickness of the cornea (Fig. 150). These are infiltrated and undergoing necrosis. Near this edge there are blood-vessels between the lamellæ; beyond it, Bowman's membrane is destroyed for a short distance.

The ulcers have been examined for micro-organisms, and Andrade has described a specific bacillus. The bacilli are small mobile rods, sometimes lying side by side, sometimes grouped as diplobacilli, or forming long chains. They are coloured by Gram's method, and liquefy gelatine and Löffler's blood-serum. They grow with difficulty on agar; they do not produce indol; they require oxygen to grow well. I have taken cultures from several cases of Mooren's ulcer, but have failed to obtain Andrade's or any other specific organism.

MOOREN.—Ophthalmiatrische Beobachtungen, 1867; Ophthalmologische Mittheilungen, 1873. LAWFORD.—R. L. O. H. Rep., xii, 3, 1889. KREY.—Inaug. Diss., Kiel, 1890. HILLEMANNS.—A. f. A., xl, 1899. SCHMIDT-RIMPLER.—A. f. A., xxxviii, 1899; A. of O., xxx, 1901. ANDRADE.—Ann. di Ott., xxix, 1900. * NETTLESHIP.—T. O. S., xxii, 1902. LISTER.—R. L. O. H. Rep., xv, 1903.

DEGENERATIONS

DEGENERATIVE CHANGES IN THE EPITHELIUM

We have already considered the degenerative changes which occur in the epithelium from œdema (p. 175), from the improper use of cocain (p. 203), in various types of pannus (p. 194), etc. There are a few other conditions which require consideration, more particularly those resulting from malnutrition and desiccation.

There may be little change in the epithelium over a primary focus of infiltration (Fig. 152).

Insufficient nutrition may lead to atrophy of the epithelium, manifesting itself by diminution of the number and size of the cells. The superficial flat-cells lose their nuclei and become thin scales, the middle polygonal cells are changed into flat ones, which lie immediately upon the cylindrical foot-cells (Fig. 153). Later on these too become shorter, oblique, and finally flat (Figs. 154, 155), and in the highest degree of atrophy the epithelium fades gradually away (Figs. 153, 155). Thinning by atrophy is most seen in cicatricial conditions of the cornea, especially when combined with calcareous deposits. The scar tissue has probably increased resistance to the invasion of organisms, owing to the absence of lymph-channels and the occasional presence of blood-vessels. This is not sufficient to protect the tissues invariably, as is shown by the occurrence of atheromatous ulcers (*v.* p. 221). Malnutrition causing atrophy may be due to local causes, *e. g.* tuberculosis of the iris and ciliary body (Fig. 154), or to general causes, *e. g.* in keratomalacia.

Circumscribed necrosis of the epithelium may occur in an otherwise normal cornea after irritation (Fuchs). After cataract extraction minute grey spots may sometimes be seen in the cornea near the

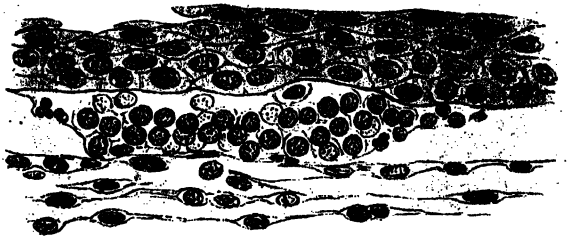


FIG. 152.—PRIMARY KERATITIS.

Fuchs, T. O. S., xxii. Comparative freedom from change of the epithelium in primary keratitis. Bowman's membrane is infiltrated and destroyed in the centre of the figure.



FIG. 153.—ATROPHY OF EPITHELIUM.

Fuchs, T. O. S., xxii. Thinning off of the epithelium, with diminution in the number of the cells, and formation of thin scales, devoid of nuclei. The basal cells become shorter and oblique.

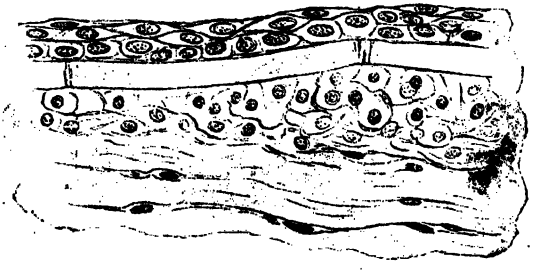


FIG. 154.—ATROPHY OF EPITHELIUM.

Fuchs, T. O. S., xxii. From a case of tubercle of the iris and ciliary body in a child. The basal cells have become quite flat and are directed horizontally. Bowman's membrane is intact. The superficial lamellæ are swollen and jelly-like, with an increased number of nuclei.



FIG. 155.—ATROPHY OF EPITHELIUM.

Fuchs, T. O. S., xxii. From near the margin of a corneal infiltration. The epithelium thins off and disappears. Bowman's membrane is intact.



FIG. 156.—ATROPHY AND NECROSIS OF EPITHELIUM.

Fuchs, T. O. S., xxii. The superficial layers are necrotic, being changed into a nearly homogeneous mass, devoid of nuclei. Such appearances are found near corneal ulcers.

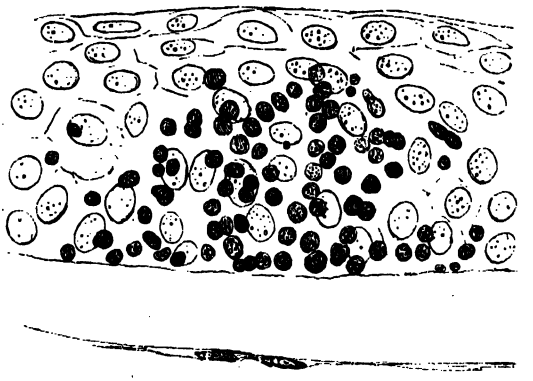


FIG. 157.—INFILTRATION OF EPITHELIUM.

Fuchs, T. O. S., xxii. Infiltration of a localised spot of epithelium with round-cells, Bowman's membrane and the subjacent cornea being intact.

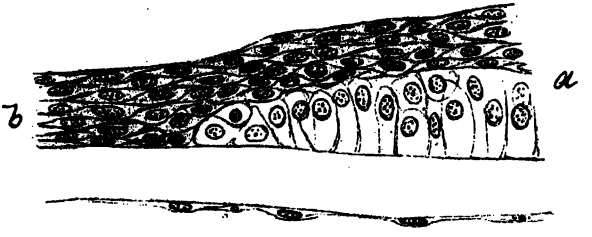


FIG. 158.—DESICCATION OF EPITHELIUM.

Fuchs, T. O. S., xxii. Margin of uncovered cornea in lagophthalmos. (For explanation, *see* Text.)

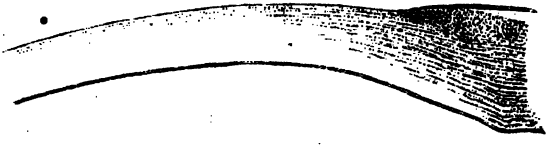


FIG. 159.—TOTAL EXFOLIATION OF EPITHELIUM.

Fuchs, T. O. S., xxii. From a case of commencing panophthalmitis. Total exfoliation of epithelium and endothelium; necrosis of substantia propria, as shown by absence of stained nuclei.

margin, especially near the incision. They may develop to very small ulcers, but generally disappear in a day or two. They are probably small foci of epithelial necrosis due to the action of cocain, sublimate, etc. A small opaque spot may also correspond with an inflammatory infiltration with lymph-cells, limited entirely to the epithelium (Fig. 157).

Fig. 158 shows the effect of drying. In *a* the desiccation affects only the superficial layers. If the basement-cells resist, the epithelium will be preserved; the superficial cells will lose their nuclei, or become keratinised (*v.* p. 170), whilst the basement-cells, in consequence of the irritation, will increase their proliferating activity, and the epithelium will become thickened. If the desiccation goes deeper, as in *b*, the basal cells are also destroyed, and will be thrown off.

After prolonged exposure the epithelium becomes epidermoid in type, exactly resembling that of the skin. This occurs in the cornea in anterior staphyloma (p. 170), as well as in the conjunctiva in xerosis, etc. (p. 103).

Finally the whole epithelial covering of the cornea may be cast off. This takes place typically in neuro-paralytic keratitis. It is also found in acute disease affecting the eye as a whole, *e. g.* panophthalmitis. Here the desquamation is part of a more extensive process involving the whole cornea. In Fig. 159 the posterior endothelium has been destroyed, and more than two-thirds of the substantia propria exhibit not a single stained nucleus, proving thus their complete necrosis. Only in the anterior still living layers of the cornea an infiltration has taken place, and the epithelium has been thrown off entirely. Similar changes are found in other cases of partial or complete necrosis, *e. g.* ring infiltration (q. v.), necrosis *en masse* (q. v.), etc. The damaging of the epithelium by the influence of the aqueous humour may become manifest also in slighter cases, where in the cornea itself no disturbance may be manifest.

Fuchs.—T. O. S., xxii, 1902.

Hyaline Deposits (Drusen) on Bowman's Membrane

Bowman's membrane, being a specially differentiated part of the substantia propria, is not a hyaline membrane derived from epithelial or endothelial cells. Very rarely hyaline deposits are seen upon it, resembling those which occur upon Descemet's and Bruch's membranes.

They were first described by Rindfleisch (1891) as swollen, greyish, transparent spots in a congenitally defective eye. Bowman's membrane in the middle of the cornea was scarcely distinguishable from the hyaline substantia propria; on its surface were several small hemispherical thickenings, uniting with it and staining in the same manner.

Leber (1897) described nodules on Bowman's membrane in band keratitis (q. v.). These are identical with the hyaline deposits found in "colloid" degeneration (q. v.), and are different from the typical hyaline deposits which are confined to Bowman's membrane.

Only one quite typical case has been described, viz. by Elschnig

(1899). The deposits occurred in the almost normal eye of a man with chronic lead-poisoning, and were detected by the irregular refraction of the surface of the cornea. By oblique illumination irregular reflexes were seen, as if caused by globular drops of different refrangibility from the surrounding media. Microscopically there were rows of smooth, hemispherical, homogeneous deposits on the surface of Bowman's membrane. The epithelium over them was thinned at the summit, so that the surface of the epithelium remained smooth. The smallest "Drusen" were less than the thickness of Bowman's membrane, whilst the largest were somewhat laminated, and were two to two and a half times as thick. The larger the deposits the more sharply they were defined, a small cleft being visible below some of them. With hæmatoxylin and eosin they stained deeper than Bowman's membrane, with van Gieson a paler yellow, paler blue with thionin, deeper with saffranin, nigrosin, and Weigert's elastic-tissue stain; they remained unstained with iodine, acid orcein (Unna-Tänzer), and Meyer's muc-hæmatein. They are therefore not amyloid, but must be relegated to the indeterminate hyaline deposits. Elschnig regards them as products of the epithelium, the main argument against this view being the nature and origin of Bowman's membrane. In all probability Bowman's membrane has nothing to do with their actual development; they merely lie upon it. It is quite possible that they may be degeneration products of exudates, which are not infrequently found in this situation, and the general condition of the patient (lead-poisoning) is rather in favour of this view than of an epithelial origin.

Rindfleisch.—A. f. O., xxxvii, 3, 1891. Leber.—B. d. o. G., 1897. * Elschnig.—K. M. f. A., xxxvii, 1899.

Hyaline Deposits (Drusen) on Descemet's Membrane

It has already been mentioned that Descemet's membrane increases in thickness with age. Localised hemispherical thickenings, protruding upon the posterior surface, are not uncommon, and were first described by Hassall and Henle. They commence at the periphery, usually at about twenty to thirty years of age, and are always most marked here. They project 3—5 μ above the surface, forming two to four incomplete rows, which increase in number later in life, and may rarely involve the whole area, seldom projecting more than 10—12 μ. They may thus become visible macroscopically, and may be mistaken for punctate opacities. Like the membrane itself they are the products of secretion of the endothelial cells (Leber), and are in all respects comparable with the "colloid" bodies of the choroid, and may, like them, become calcified. The endothelial cells usually remain in the depressions between the excrescences, forming star-shaped figures. Care must be taken not to confound oblique sections of Descemet's membrane, artefacts from inefficient hardening, etc., with these new formations.

Hassall.—The Microscopic Anatomy of the Human Body. Henle.—Handbuch der syst. Anat., ii, 1866. Leber.—A. f. O., xxv, 3, 1879. Waldeyer.—In G.-S., i, 1874; and in de Wecker and Landolt's Traité, ii, 1886.

Arcus Senilis

Very various opinions have been expressed from time to time as to the pathological changes in the cornea in arcus senilis.

Canton first accurately described the microscopic appearances. His careful description (well illustrated in his book) is as follows:—"With a power of 200 diameters we shall observe myriads of fine oil-globules in the situation of, and constituting the arcus. Many larger globules are present, and this magnitude has doubtless been attained by the coalescence of the smaller spherules. We notice also that the oil-drops are arranged in two ways:—First, in the direction of such of the

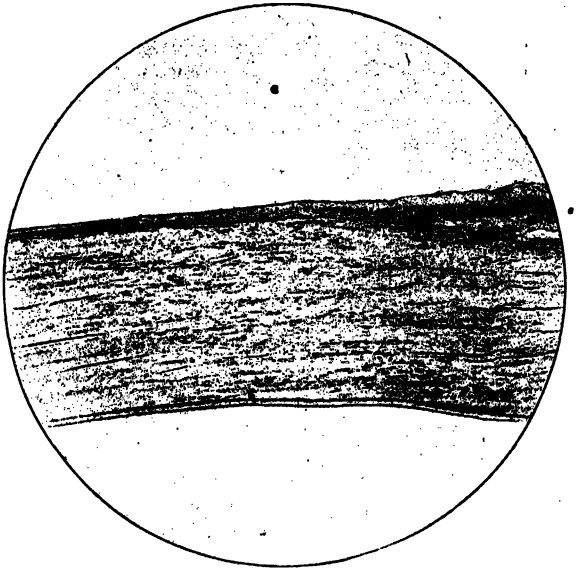


Fig. 160.—Arcus Senilis. × 55.
Stained by hæmatoxylin and Scharlach R. Note the distribution of the fatty globules (*see* Text).

lamellæ as have disappeared, and which they replace—a fatty degeneration or conversion, and second, in the interstices, or between the lamellæ—a fatty deposition. The slight elevation which the cornea presents at the site of the arcus is due to this latter condition.

"At the commencement of these changes the oil-drops will be found in the corneal cells, and often, too, are present in the fine branches or processes prolonged from these cells; in the same manner as the contents of the cellular elements of other organs are, primarily, affected where fatty degeneration occurs, and where, in the further progress of the affection, we may notice also the intercellular deposit." . . . .

"I have never seen Bowman's membrane (anterior elastic lamina) nor that of Descemet (posterior elastic lamina) to be otherwise than unaltered." . . . .

"With respect to the rim of cornea lying just external to the true arcus, and which, as a general rule, is unaffected, it will be not unfrequently found, in instances where an arcus is very broad, or a dense circle exists, that this part has become implicated also to a greater or less degree by a continuity of fatty degeneration from the arcus itself. This occurs more commonly above and below, than at the sides of the cornea." . . . .

"I have in some cases found the fatty degeneration to extend completely into the line of junction of cornea and sclerotic; and have occasionally seen the interstices of the sclerotic fibres as they are becoming corneal laminæ, in many places, loaded with oil-drops."

His says: "If thin sections through an arcus senilis are examined, the fat is principally found to consist of extremely fine globules, which are arranged in thickly set parallel thread-like rows. These parallel rows cross in various directions and so form a kind of thick network, which, when it is many layers thick, causes considerable opacity in the tissue. In some places large groups of globules are collected, in the midst of which one or more stunted rudiments of a nucleus may occasionally be seen. These fat-drops have no capsule, and it is impossible to prove from their appearance only that they correspond to a degenerated corneal corpuscle. On the other hand, there are undoubtedly corneal cells with more or less fat within them, especially in the more posterior layers and in the parts where the opacity is less intense. Such cells are not actually enlarged, and the fat lies partly in the cell-body and partly in the fine processes and their ramifications."

Virchow used the arcus senilis as a typical example of parenchymatous changes. He considered it a fatty degeneration of the corneal tissue, and due to deposition of fat in the cells themselves.

Fuchs, in a paper on pinguecula, says: "Concretions of the same nature as those found in pinguecula constitute the opacity of the cornea, which is called arcus senilis. Senescence of tissue leads therefore in the cornea to the same results as in the conjunctiva. . . . The greenish-coloured round concretions which form it lie for the most part immediately under Bowman's membrane. They consist of various sizes, from the smallest, scarcely visible up to 0·03 mm., mostly arranged in a single layer under Bowman's membrane. The larger concretions, by pressure on the posterior surface of Bowman's membrane, dig as it were niches in it, the largest thin the membrane very markedly and push it forwards. The concretions do not occur, however, only under Bowman's membrane; there are some which lie considerably deeper, between the corneal lamellæ. In some cases, indeed, I have only found large groups of concretions here, whilst there were none present immediately under Bowman's membrane. On the other hand, there are concretions which are found within Bowman's membrane itself or even upon it. In the first case, when the concretions are very fine, the membrane appears as if dusted over, but it may also contain larger concretions. In the second case the concretions are embedded between the cells of the corneal epithelium. There is never any relation to be perceived between the concretions and the cells of the corneal tissue; the hyaline substance is here, exactly like the yellow masses in pingue-

cula, lying separated and free upon the surface of the connective-tissue bundles (here corneal lamellæ). The concretions in the cornea give the same reactions as the concretions in pinguecula. I may here only further state that they undergo no change whatever with ether or chloroform, so that therefore they are certainly not fat, as generally held."

Leber is of opinion that in arcus senilis there is a combination of hyaline degeneration with a deposition of calcareous material. In one case he obtained the very definite calcium reaction with oxalic acid.

Tweedy writes: "According to some investigations made by the writer in conjunction with Mr. E. T. Collins, in the laboratory of Moorfields Eye Hospital, the change in the cornea consists in the presence of fine, highly refractive molecules, distributed along the course of the lymphatic spaces and channels of the superficial layers of the periphery of the cornea near the loop-endings of the capillaries of the conjunctival and episcleral blood-vessels. The greater portion of these molecules are not fatty, as is generally supposed; for, unlike fat, they are neither blackened by osmic acid nor dissolved by ether. They probably arise from mucoid degeneration of the protoplasm within the lymphatic channels and spaces of the cornea, and to some extent of the fibrillæ themselves. A few doubtful, blackened, fatty molecules may be seen here and there in sections stained by osmic acid. The fibrillæ are slightly wrinkled, and are more loosely held together than natural, and the spaces between the laminæ are wider. In support of the non-fatty nature of arcus senilis, it may be stated that wounds of the cornea, whether through the opacity, or to its inner side, or to its outer, and whether surgical or traumatic, heal in a natural way."

Takayasu, working in Greeff's laboratory, used Sudan III as a test for fat, and arrived definitely at the conclusion that arcus senilis is a fatty degeneration.

In my own experiments I have used Sudan III and an allied stain, Scharlach R. The results confirm the description of Takayasu, and I have extended the observations by employing the stains as chemical indicators of the presence or absence of the arcus after the action of various reagents.

When stained with either of the dyes, the smaller globules are coloured reddish yellow, the larger ones deep orange. With Scharlach R the stain has a brick-red tinge. The eyes were hardened in formol, the corneæ, including the iris and ciliary body, being then removed by a circular incision through the sclerotic 2 or 3 mm. behind the corneo-scleral margin. The corneæ were then divided into quadrants, washed in running water to remove the formol, immersed in gum until penetrated, and cut with the freezing microtome. After being freed from gum by warm water, sections were placed in saturated solutions of the stain in 70 per cent. alcohol. Stronger solutions of alcohol dissolve out the globules. In Sudan III the sections are well stained in from ten to fifteen minutes; longer treatment leads to slight diffuse staining of the corneal tissues, but this is washed out in subsequent treatment with 70 per cent. alcohol. It is possibly due to a fatty moiety in more stable combination in the normal tissues, for traces of fatty material can be extracted from

almost every tissue of the body. Scharlach R stains more slowly, but does not tend to diffuse staining, even after prolonged (twenty-four hours or more) treatment, and is therefore a more reliable test of differentiation. The sections after staining are washed rapidly in 70 per cent alcohol, a more prolonged differentiation being required in sections over-stained by Sudân III. They are then washed in water, and counter-stained with Meyer's hæmalum or Ehrlich's hæmatoxylin. This stains the nuclei of the corneal corpuscles, etc., and to some extent delimits the corneal fibres. Hæmalum is preferable, as it is a pure nuclear stain; it may precede the treatment with the fat stain. The sections are then treated with tap-water until the hæmatoxylin is a satisfactory violet, and are mounted in glycerin.

In sections so treated, globules of varying size are seen to pervade Bowman's membrane and the corneal lamellæ in the affected area. (Fig. 160). Those in Bowman's membrane are usually the smallest, so small, indeed, that a general diffuse granular stain is all that is seen without the assistance of an oil-immersion objective. A few minute, isolated, well-defined gloubles may be seen in some cases. The stain is densest at the termination of Bowman's membrane, and this is the cause of the very definite peripheral edge of the arcus, as seen clinically. Bowman's membrane ends at an appreciable distance from the apparent corneo-scleral margin, and this distance is occupied by the clearer cornea, which is characteristic of arcus senilis. That it is not in reality as clear as the centre will be evident from subsequent remarks. Towards the centre of the cornea the stain in Bowman's membrane very gradually fades off, the distance varying with the development of the arcus in the particular cornea. It always, however, extends farther centrally than the stain in the substantia propria.

In the substantia propria the globules are limited to the lamellæ and corneal corpuscles, and are not contained in the lymphatic spaces and channels. The droplets are usually larger than those in Bowman's membrane, but the finer punctate appearance is seen around the larger drops. The largest drops are from 5—10 μ in length, and about half the width, the long axis being in the direction of the lamellæ, *i. e.* more or less concentric with the surface of the cornea. This is due doubtless to the conditions of tension of the tissues. The smaller globules also show a similar disposition to be arranged in layers in the same direction; they are invariably punctate or spherical.

Tangential sections demonstrate that minute drops are also contained in the cytoplasm of the corneal corpuscles, extending into the processes of the cells, and showing a polar arrangement near the nucleus, as pointed out by His and Virchow.

Immediately beneath Bowman's membrane the stain is limited to the same extent, but each succeeding lamella is affected a little farther towards the periphery, so that in transverse sections a kind of staircase arrangement is seen. The deeper layers are usually less affected towards the centre of the cornea, and the density of the deposit also diminishes from before backwards, so that the middle layers of the substantia propria are little stained or not at all. Even under these circumstances, however, there is a further increase in the deepest

layers, but the stain is not distributed here so uniformly, with the single exception that it is invariably extremely dense upon the surface of Descemet's membrane. With a low power, and particularly in thick sections, Descemet's membrane seems to be much involved, but with a higher power, and in thin sections, it is obvious that it escapes entirely in reality, the dense deposit being only upon the anterior surface.

It is therefore obvious that the clearer peripheral ring of cornea is not entirely unaffected, but is comparatively clear, owing to the absence of Bowman's membrane and the slighter implication of the more superficial layers of the substantia propria due to the staircase arrangement.

Beyond the true corneal margin there is a limiting area of sclerotic which I have never seen affected. Beyond this, however, there is frequently some deposition of fatty material in the deeper layers of the sclerotic.

Slight deposition of fat is almost invariably seen in the roots of the ciliary processes. This is probably physiological.

Using Sudan III or Scharlach R as indicators, it is found that the material is insoluble in water, dilute acetic acid, Müller's, Marchi's, Flemming's, and Hermann's solutions, etc., and that it is soluble in absolute alcohol, ether, chloroform, xylol, etc. Thus, after staining with Sudan III and immersion for half a minute in absolute alcohol, scarcely a trace of the stain remained, no globules could be seen, and the lamellæ had the appearance of normal lamellæ. Similar treatment for half a minute in ether resulted in total disappearance of the stain and the arcus. Hence arcus senilis cannot be demonstrated in paraffin or celloidin sections.

The globules can be dissolved out and restained upon the slide. Thus, a section was stained with Sudan III and mounted in 70 per cent. alcohol, covered with a cover-glass, and watched under the microscope. A small quantity of absolute alcohol was placed upon one side of the cover-glass and drawn through by means of blotting-paper. This was followed by a small dose of ether. The stain was rapidly dissolved out. The section was then restained with Sudan III upon the slide, the ether having evaporated. Many oil-globules were seen hanging about the anterior surface of the epithelium, well stained by the dye.

Fresh sections were stained by various solutions containing osmic acid, for varying lengths of time. No definite staining was obtained with 2 per cent. osmic acid, unless it was allowed to gradually dry, in which case the whole section became black. It is known that osmic acid acts best after previous treatment of the sections with hardening reagents—2 per cent. osmic acid, after treatment of the section with 70 per cent. alcohol, failed to stain the deposit. Sections were placed in large quantities of Marchi's solution, Flemming's solution, and Hermann's solution, and examined at intervals from twenty-four hours to three weeks, being mounted in glycerin. In no case was there any true reduction of the osmic acid. The neighbourhood of the arcus certainly showed a blackish appearance, but this was apparently due to a difference in the relative refractility of the globules and the surrounding tissues, for under a high power it was seen that the black-

ness disappeared on slight alterations of focus. Further, after such treatment the arcus readily dissolved out when treated with ether, leaving no trace behind; and the blackened sections, when mounted in Canada balsam in the usual manner, could not have been distinguished from normal corneæ. There can therefore have been no true reduction of the osmic acid.

Fresh sections were treated by Bolton's modification of the Weigert-Pal method;[1] *i. e* they were placed in 1 per cent. osmic acid for a few minutes, then in ammonium molybdate solution overnight, stained black with Kultschitzky's hæmatoxylin, and differentiated in Pal's solution. By this means the arcus was stained black. The stain was removed on treatment with ether.

Experiments were made to see if the globules contained phosphorus. For this purpose, Macallum's very accurate modification of Lilienfeld and Monti's method was used.[2] Sections were immersed in ammonium molybdate solution for twenty-four hours in an incubator at 35° C.; they were then dipped in 4 per cent. solution of phenylhydrazin hydrochloride, washed in water, stained in Sudan III, and mounted in glycerin. The distribution of phosphorus in the tissues was admirably shown. The arcus showed no trace, but was well stained by the Sudan III. Sections similarly treated, but not counterstained with Sudan III, also showed the absence of phosphorus from the globules.

On the hypothesis that the material was fatty, an attempt was made to saponify the fat upon the slide. The section was mounted, without covering, in 70 per cent. alcohol. A small piece of metallic sodium was then placed in the fluid near the section and the reaction watched under the microscope. By this means sodium ethylate (C_2H_5·ONa), with sodium hydrate (NaOH), was produced. The former is capable of saponifying fats in the cold. A large crop of acicular crystals (? C_2H_5·ONa) was formed, and the globules of the arcus disappeared.

Fresh sections stained with Lugol's solution (iodine dissolved in 1 per cent. solution of potassium iodide) stained the globules yellow, as is the case with most tissues. There was no trace of amyloid reaction.

Canton's statement that Bowman's membrane is unaltered is inaccurate; as shown above, it is the main cause of the densest part of the arcus senilis.

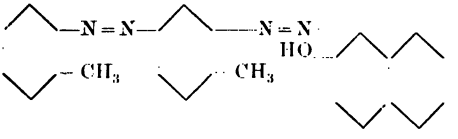
He further states that there is a slight elevation of the cornea at the site of the arcus. This is also inaccurate; but there is an undoubted, though usually slight, diminution in the thickness of the cornea peripheral to the arcus. The contrast probably led to the error. This slight thinning of the cornea outside the arcus points to a condition of sclerosis as a constant accompaniment of the degeneration. If this be so, it is interesting in connection with those rare cases of peripheral sclerosis and peripheral atrophy (Randsclerose and Randatrophie) which Fuchs has recently described, and which only occur in association with a previously established arcus senilis (*v.* p. 247).

It is difficult to reconcile my observations with those of Fuchs and

[1] BOLTON, Jl. of Anat. & Phys., xxxii; Z. f. wiss. Mikr., xv.
[2] MACALLUM, Jl. of Phys., xxiii, Supplement.

Leber, but in all probability they examined cases in which other degenerative changes were present, masking the true arcus, which would have disappeared in the specimens mounted in Canada balsam.

The conclusions arrived at by Tweedy and Treacher Collins are chiefly explicable by the behaviour of the globules to osmic acid. Even Takayasu, whose results I confirm for the most part, states that the globules stain with osmic acid, though with difficulty. I agree that they become blacker, but this is no evidence of a true fat stain, for I have proved that the osmic acid is not reduced. This result introduces a complication into the explanation of the action of Sudan III and Scharlach R. It has been shown by Altmann and others[1] that osmic acid only stains, *i.e.* is only reduced by fats which are glycerides of the chemically unsatisfied acrylic series of acids (C_nH_{2n-1}·COOH, of which olein is the commonest representative in animal tissues. Sudan III was first used by Daddi,[2] the idea of its utility for microscopic purposes being derived from the fact that it was used commercially for staining fatty preparations, *e.g.* pomades, etc. The nature of the dye and of its congener Scharlach R, which is chemically azo-orthotoluol azo-β-napthol—



(Sudan III having the same formula, except that the two H's have not been replaced by (CH_3) groups) has been worked out by Michaelis.[3] He explains their action upon the same principle as that of osmic acid, viz. that reduction of the stain is brought about by the action of fatty acids of the acrylic series. If this is true we should expect osmic acid, Sudan III, and Scharlach R to invariably act in the same manner. This is not the case with arcus senilis, and we are forced to the conclusion, either that there is some flaw in the chemistry of the action of these stains, or what is more probable, that osmic acid is more stable than the aromatic stains, which are reduced by a smaller amount of, or by less potent members of, the acrylic series.

It was thought possible, on account of the common occurrence of cholesterin in senile degenerations, that the fat-like material might be a cholesterin ester, or ethereal salt of a fatty or other acid. These bodies occur in large quantities in lanoline. The supposition was improbable *à priori*, for most cholesterin esters are insoluble in alcohol. On saponification they are split into the acid and cholesterin, which is an alcohol with the formula $C_{27}H_{45}$·OH. It was just possible, if they were present, that cholesterin would crystallise out in its typical form upon the slide, when the section was treated with sodium ethylate. This, however, did not occur.

Most fats are not readily soluble in alcohol, and the globules of the

[1] *See* Handwerck, Z. f. wiss. Mikr., xv.
[2] Daddi, Arch. ital. de Biol., xxvi.
[3] Michaelis, Virchow's Archiv, clxiv.

arcus senilis show less solubility in it than in ether, but probably more than most fats.

In conclusion it may be stated that the arcus senilis is probably a fatty degeneration of the substantia propria of the cornea, the exact chemical nature of the fatty material being still undetermined.

CANTON.—Lancet, 1850; The Arcus Senilis, London, 1863. WILLIAMS.—Quoted by Canton, p. 18. HIS.—Beiträge zur nor. und path. Anat. der Cornea, Basel, 1856. VIRCHOW.—Virchow's Archiv, iv, 1852. FUCHS.—A. f. O., xxxvii, 3, 1891. LEBER.—In Vossius, Lehrbuch. TWEEDY.—Quain's Dict. of Med., art. "Arcus Senilis." TAKAYASU.—A. f. A., xliii. PARSONS.—R. L. O. H. Rep., xv, 2, 1902.

FATTY INFILTRATION AND DEGENERATION

Fatty infiltration and degeneration of the cornea occurs typically in the form of arcus senilis (q. v.). It has also been described occasionally in other conditions, in the form of large globules (Baumgarten), and in large aggregations in widened lymph-spaces, recalling the histological features of xanthelasma (Kamocki). Probably it is frequently overlooked, owing to the routine methods of embedding eyes for examination, the fat being dissolved out by the reagents used.

BAUMGARTEN.—A. f. O., xxii, 2, 1876. KAMOCKI.—A. f. O., xxxix, 4, 1893.

HYALINE, COLLOID, AND AMYLOID DEGENERATION

Deposits of hyaline substances, which give various staining reactions, are common in old leucomata, anterior staphylomata, band-shaped opacity (q. v.), etc. They look deep yellow to the naked eye, and may project above the surface. They are usually limited to the superficial layers, and appear microscopically as homogeneous, highly refractile globules (Fig. 161). The earliest deposits are minute granules; these coalesce into round globules, and finally into large masses, which usually show their mode of growth by accretion in their crenate edges. The material is very insoluble, resisting most reagents, except concentrated alkalies and acids. They stain deeply with acid fuchsin and methylene blue, partially or not at all with hæmatoxylin and carmin. Weigert's fibrin stain colours the granules, not the larger globules, or only at the edges. Weigert's elastic-tissue stain colours the larger globules red. They stain deeply with Weigert's and Pal's medullary stains. Russel's and Gabbet's stains colour the granules deep red, the cells greenish blue or blue. van Gieson's stain colours the deposits variously—yellow, orange, or brown. The variety of the staining reactions shows clearly here, as elsewhere, in the conjunctiva, etc., that we are dealing with no stable chemical body. This is further shown by the fact that the amyloid reactions are sometimes given quite typically, but far more frequently in an indefinite manner, or not at all (*v.* p. 96).

These deposits have long been known and figured (de Vincentiis, Saemisch, Goldzieher, Wedl and Bock). Beselin was the first to demonstrate amyloid in the cornea of a staphylomatous eye. It has

since been found by E. von Hippel in two eyes. Kamocki regarded the material as identical with v. Recklinghausen's "hyalin" in his observations. Baquis prefers the term "colloid," defining it as a substance which is very closely related to amyloid. The theory of the conversion of "hyalin" into amyloid has been discussed elsewhere (*v.* p. 96). Birch-Hirschfeld, dealing with the cornea, sums up in favour of three stages: (1) giving the staining reactions of fibrin; (2) giving the hyalin or colloid reactions; (3) giving the amyloid reactions.

Baquis was able to examine an early and progressive condition. The epithelium was implicated as well as the substantia propria, fine granules appearing in the cells in the first stage, staining with fuchsin



FIG. 161.—BAND-SHAPED OPACITY. × 90.

The dark amorphous and globular masses near the surface consist of hyaline material. There were calcareous deposits in the same situation elsewhere. The middle layers of the substantia propria are infiltrated and vascularised.

from the beginning. The intercellular spaces were often filled with colloid material, and the cells had often run together, and were surrounded by a ring of the substance. The corneal cells also take part in the formation of colloid. At the periphery of the affected area the lymph-channels were distended with clear fluid, and the cells were flattened or swollen, and often devoid of nuclei. Elsewhere were transitions to masses of granules in the channels; these stained more and more deeply with fuchsin, and finally ran together into homogeneous globules.

Birch-Hirschfeld examined four cases. The epithelium was normal in the peripheral parts and in some places where there were already deposits in the anterior layers of the substantia propria. Nearer the

centre it was much thickened, with conical downgrowths into the connective tissue. Here Bowman's membrane was absent, and the downgrowths were surrounded by loose, richly cellular connective tissue. Groups of epithelial cells were arranged concentrically or spirally. Between the epithelium and the fibrous tissue, and in the epithelium itself, were deposits, stained bright yellow by van Gieson. They were chiefly sickle shaped, with the convexity towards the surface; others were flat or spindle shaped. They were quite homogeneous, without any lamination. Only a few of the smaller granules and globules were seen in the epithelium, and these were all between the deepest cylindrical cells; they were undoubtedly extra-cellular. Many epithelial cells were necrosed, and had fused into a finely granular cellular

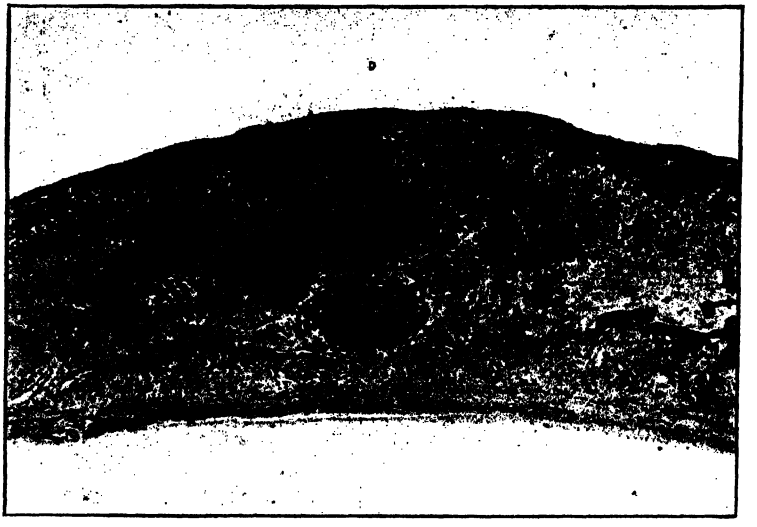


FIG. 162.—HYALINE DEGENERATION OF SCAR TISSUE. × 34.

From the same specimen as Fig. 108. The cornea was white and gelatinous. The epithelium is very irregular, with vesicles in many parts. The substantia propria is transformed into whorls and masses of hyaline material, with a few leucocytes and small blood-vessels in places.

detritus, in which a few nuclear granules stained with hæmatoxylin. A special modification of van Gieson, in which the sections were previously stained for ten minutes with 3 per cent. picric acid fuchsin, was held to prove that the deposits were not derived from the broken-down cells. Nowhere in the sections was any protoplasmic ring or cell-membrane to be seen around the globules, such as was described by Leber in amyloid deposits in the conjunctiva, and confirmed by v. Hippel. The epithelial deposits were proved by serial sections to be continuous with those in the connective tissue, the insular nature of the deposits being only apparent. The crescentic shape of the deposits is best explained on the theory that fluid passed from the connective tissue into the epithelium, lifting it up and separating the cells. It

then coagulated and became degenerated into hyaline masses. That such a process is possible, especially after the destruction of Bowman's membrane, is shown by the injection experiments of Leber[1] and Raehlmann.[2]

The sub-epithelial new connective tissue consisted of rich networks of fibrillæ, with rod-shaped nuclei, and dilated blood-vessels. The globules occurred isolated and in long rows between the bundles of fibrils; they were chiefly spherical, the smallest being about the size of a red corpuscle. In places they seemed to form a continuation of the fibrils themselves, as if derived from them, and this view is supported by granules within the corneal lamellæ. Here, again, there was no evidence of their derivation from the cell-elements. Only a few wandering cells were present.

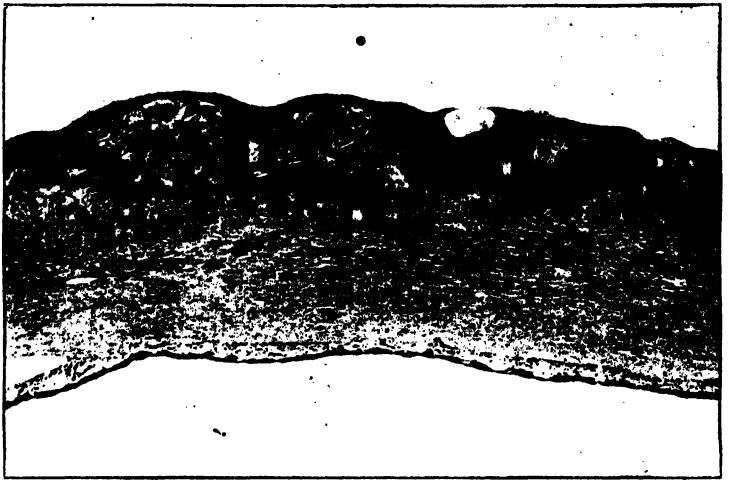


FIG. 163.—HYALINE DEGENERATION. × 34.

From a partial anterior staphyloma. The scar tissue on the surface is transformed into whorls and clumps of hyaline material, which contains calcareous salts in parts. The masses are pushed up into the epithelium, which is thus made very irregular, though the levelling tendency is still apparent. Towards the right is a vesicle in the epithelium, containing hyaline substance. The deeper layers of the substantia propria are infiltrated and vascularised. Below is the adherent degenerated iris.

Sachsalber lays stress upon the conditions found in the epithelium, some of which were described by Birch-Hirschfeld. Besides the usual degeneration there is very frequently a network of strands composed of horny cells, growing down into the deeper layers of epithelium. Whorls of epithelial cells are also formed around the concretions; many of the inner cells are flattened and look like connective-tissue cells. The sub-epithelial connective tissue also invades the epithelium, and may lead to the isolation of groups of epithelial cells, which

[1] LEBER, A. f. O., xiv.
[2] RAEHLMANN, A. f. O., xxiii, 1.

gradually disappear, and are replaced by concretions. Patches of softening occur in the epithelium, leading to the formation of cystic spaces.

Various theories have been put forward to account for these hyaline masses. There can be no doubt that the fundamental condition is one of malnutrition, and probably desiccation plays some part in the process. de Vincentiis regarded the substance as derived from the cells, Beselin from the lamellæ and connective-tissue fibrillæ, it passing subsequently between the epithelial cells. Kamocki thought the process a hyaline degeneration of the corneal cells or scar tissue. E. v. Hippel ascribed the material to slow degeneration of extravasated blood. Baquis considered it partly a secretion product of the living cells, including the epithelium, partly a degeneration product of necrosed cells and red and white corpuscles, and partly altered exudate. Birch-Hirschfeld held that ferments produced by cell necrosis led to coagulation of fluid derived from the blood, the whole process being intercellular.

Best has brought forward further evidence that the deposits are altered proteid material, most allied to the tyrosin component. With Millon's reagent, even in the cold, they are coloured deep brownish red; but they are not pure tyrosin, as shown by their form, the absence of red colouration with sulphuric acid, and the absence of sulphur reaction. If sulphur is present it is in such stable combination as to give no reaction with basic lead acetate. They also contain the uric acid radicle, as shown by their giving the biuret reaction. They do not contain a carbohydrate molecule, since the Adamkiewicz and Molisch reactions are negative. Glycogen is absent, though it occurs in other hyaline deposits in the eye.

Sachsalber considers that the concretions arise in the scar tissue and corneal stroma, and only extend secondarily into the epithelium; he regards them as solely extra-cellular.

There can be little doubt that this view is on the whole correct. The extrusion of the exudates and fully formed concretions leads to thinning of the epithelial covering, which retains as long as possible its smooth surface. Later the concretions may be cast off into the conjunctival sac, but this probably seldom occurs before calcification has taken place. The spot is thus denuded of epithelium, and a path is thrown open for infection (*v.* p. 221).

Besides this special type of hyaline degeneration, simple hyaline degeneration of scar tissue also frequently occurs (*v.* Figs. 108, 162, 163).

DE VINCENTIIS.—Contrib. alla Anat. path. dell' Occhio., Napoli, 1873; Lavori della Clin. ocul. di Napoli, iv, 1896. SAEMISCH.—In G.-S., iv, 1876. GOLDZIEHER.—C. f. A., iii, 1879. BESELIN.—A. f. A., xvi, 1886. KAMOCKI.—A. f. A., xxv, 1892. E. v. HIPPEL.—A. f. O., xli, 3, 1895. DE LIETRO VOLLARO.—Lavori della Clin. ocul. di Napoli, iv, 1896. LEBER.—B. d. o. G., 1897. BAQUIS.—A. f. O., xlvi, 3, 1898. BIRCH-HIRSCHFELD.—A. f. O., xlviii, 2, 1899. BEST.—B. z. A., xliii, 1900. SACHSALBER.—B. z. A., xlviii, 1901.

CALCAREOUS DEGENERATION

Calcareous deposits occur in the cornea under similar conditions to hyaline deposits (*see* "Band-shaped Opacity"). Like them, they are found in the superficial layers, most frequently on Bowman's membrane or

between the lamellæ of the substantia propria (Fig. 164). They form fine granules when first deposited, and later laminæ, or round and irregular nodules of various sizes. They often occur combined with hyaline deposits. The walls of new-formed vessels may also be hyaline or calcareous.

The calcareous parts stain deeply and diffusely with hæmatoxylin and stains containing alum. This occurs also after decalcification if, as is usual, the material is in intimate organic combination. The calcium salts found are the carbonate and phosphates. The former gives off gas bubbles with acids, and forms the typical "envelope" crystals with oxalic acid. The actual amount of calcium salts present is often extremely small, so that it is quite possible to cut thin sections without previously decalcifying. In this respect the cornea differs from

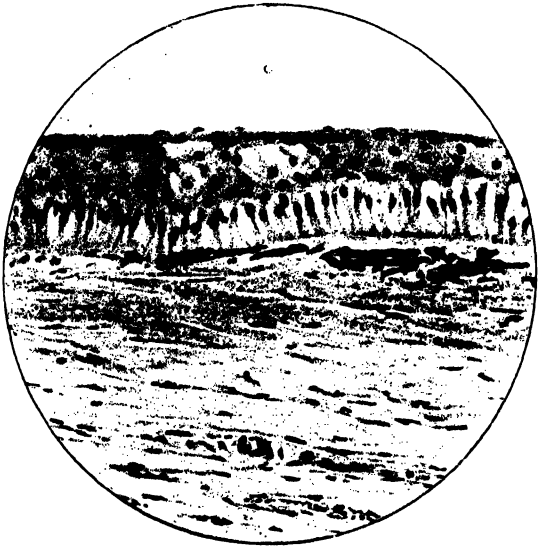


FIG. 164.—CALCAREOUS DEPOSITS IN THE CORNEA. × 200.

The basal cells of the epithelium are elongated and vacuolated; there is some vacuolation of the middle layers. The tension of the eye was sub-normal. Below the epithelium are plaques of calcareous material, deeply stained with hæmatoxylin. Below these are the earliest dusty deposits of calcareous salts. At the lowest part of the figure are several blood-vessels, containing red corpuscles.

the choroid. Consequently it may be impossible to demonstrate the presence of the carbonate by gas bubbles given off with acids in sections under the microscope. Larger pieces usually show them plainly. The lime salts are generally deposited upon an albuminous basis, and when this is dissolved by alkalies the deposits are seen to clear up as they do with acids, but not so well.

Calcareous deposits in and on Bowman's membrane lead to its being broken up, both vertically and longitudinally, and displaced or folded. In sections it often shows a double contour. The masses are frequently pushed up into the epithelium, which is always more or less altered, and is often degenerated and atrophic. There is also often

new-formed connective tissue around the calcareous masses, due to the irritation which they set up, and this is sometimes emphasised by the presence of giant-cells.

Hyaline concretions always become calcareous eventually, but calcification also occurs by primary deposition (Leber, Sachsalber).

LEBER.—B. d. o. G., 1897. BEST.—B. z. A., xliii, 1900. SACHSALBER.—B. z. A., xlviii, 1901.

BAND-SHAPED OPACITY

Band-shaped opacity was first described by Dixon in 1848—almost simultaneously by Bowman. Dixon called it calcareous deposit or *calcareous film*, and it has since received many other names, of which the following are a selection:—*Transverse film, band- or ribbon-shaped opacity* (v. Graefe), *girdle-shaped opacity* (Arlt), *band keratitis* (Obertüschen), *symmetrical opacity* (Fairlie Clarke), *trophic keratitis* (Magnus), *zonular opacity* (Fuchs), etc. An excellent *résumé* of the early accounts up to 1879 will be found in a paper by Nettleship.

The opacity forms a grey stripe, 3—5 mm. broad, passing horizontally across the cornea a little below its centre, *i. e.* in the part corresponding with the palpebral aperture (Fig. 165). It develops very slowly, occupying years in its progress. The first parts to appear are the two ends, and these are always separated from the margin of the cornea by a narrow transparent zone. The opacity gradually spreads towards the centre of the cornea from each side; when complete the two extremities, being the oldest parts, are broadest and most opaque. It is possible the pressure of the lids may partly account for the peculiar shape and development (Treacher Collins). When examined with a loup the surface is seen to be uneven, owing to multitudes of white or grey dots.



FIG. 165.—BAND-SHAPED OPACITY. From an eye with irido-cyclitis.

The condition is found in two distinct forms: (1) a *primary* form, which is very rare, and occurs in elderly people whose eyes are otherwise quite sound; (2) a *secondary* form, which is common, occuring in eyes which are nearly or quite blind, usually from irido-cyclitis (shrunken globes, etc.). The primary form has not been examined microscopically.

Dixon, in 1848, proved the presence of calcium carbonate and phosphate in particles removed from the film. It is interesting to note that his case was one of the primary form. The earliest microscopical examination is by Nettleship (1873): the cornea showed (1) puckering of Bowman's membrane; (2) perforations in this membrane, through which passed finely wavy fibrous tissue; (3) lifting up of the epithelium

by this eruption of organised fibrous tissue. Bock (1887) first investigated the subject exhaustively. In one case he found calcareous particles on Bowman's membrane only, under which was a thin layer of spindle-cells and vessels. In two other cases the substantia propria was replaced by new connective tissue, in which lay calcareous granules and calcified vessels. Usher (1893) examined thirteen cases; he confirms the arrangement of the fibrous tissue and the presence of calcareous deposits. He points out that the cornea is usually thickest at the opacity, and that the new tissue is sometimes delimited from the substantia propria by granular bands.

Leber (1897) came to the conclusion that the deposition of lime-salts always occurred first in Bowman's membrane. In some cases

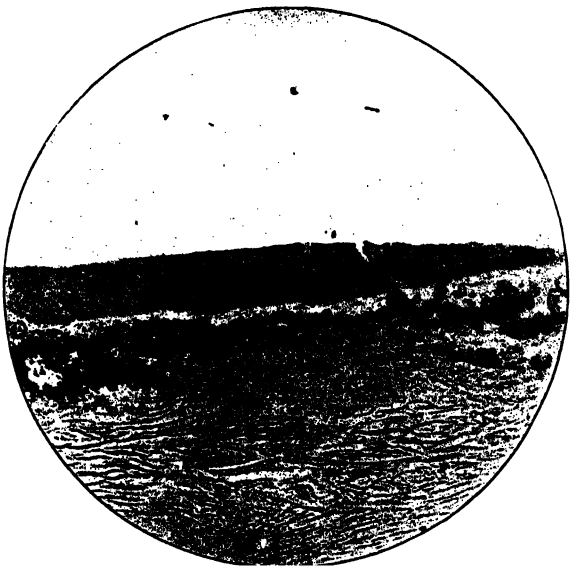


FIG. 166.—BAND-SHAPED OPACITY. × 60.

The shape of the hyaline globules, which are larger in this specimen than in Fig. 161, is well seen. Some are present in the epithelium. The stroma below is œdematous and contains very few nuclei.

the calcified membrane lay free and was covered with coral-like excrescences. He considered that it is caused by drying in the area exposed by the palpebral aperture, so that the little soluble lime-salts are precipitated; they are probably present in undue quantity, though the reason for this is not given. Leber regards the connective-tissue proliferation as secondary, and this is confirmed by a case of Schieck's, in which Bowman's membrane was calcified, but there was fibrous tissue present only in the most advanced parts.

Not only are calcareous deposits present, but also hyaline ("colloid") globules (Fig. 166). They have been observed by Bock, Goldzieher, Schrader, Kamocki, Birch-Hirschfeld, myself, and many others. They are perhaps commoner in old leucomata, but they must be regarded as

an integral part of the picture of band-shaped opacity, though this view is opposed by Greeff.

Best distinguishes three types of the condition. In the commonest sclerosing fibrous tissue is insinuated between the epithelium and the superficial lamellæ, so that Bowman's membrane is much degenerated, and often destroyed in parts, elsewhere split and fibrillated and embedded in fibrous tissue and epithelium. This fragmentation of Bowman's membrane was first described by Samter; it was found with different variations in all of Usher's thirteen cases. The epithelium is often thickened, and elsewhere thinned or destroyed, as is so frequent in these degenerative conditions. The new connective tissue is poor in vessels, or non-vascular. Occasionally giant-cells are found near the calcareous masses, induced by the irritation set up. Best, comparing the earlier marginal with the later central parts, considers the new fibrous tissue to be formed earlier beneath Bowman's membrane than between it and the epithelium.

The second type corresponds with an earlier stage, in which the band is incomplete in the centre of the cornea. Sections through this part show already a very thin layer of connective-tissue nuclei beneath Bowman's membrane, which is here very broad, as if œdematous. The thickened epithelium is raised by an albuminous exudate, which is continuous peripherally with new fibrous tissue. The condition, with the subsequent isolation and destruction of Bowman's membrane, may be compared with pannus.

The third type corresponds with Leber's description, and is not common. Bowman's membrane is uncovered by epithelium and shows coral-like excrescences. These contain a few leucocytes and nuclear fragments, but are otherwise granular. They stain by Weigert's fibrin stain, and partly by Gram, forming a strong contrast to the red, carmin-stained, calcareous Bowman's membrane. They probably consist of fibrinoid coagulum, containing the *debris* of epithelial and round-cells.

DIXON.—Diseases of the Eye, 3rd ed., p. 114, 1848. BOWMAN.—Lectures, p. 117, 1849. NETTLESHIP.—R. L. O. H. Rep., vii, 4, 1873. GOLDZIEHER.—C. f. A., iii, 1879. NETTLESHIP.—A. of O., viii, 1879. BOCK.—Zur Kentniss der bandförmigen Hornhautrübung, Wien, 1887. SAMTER.—Inaug. Diss., Königsberg, 1890. USHER.—R. L. O. H. Rep., xiii, 4, 1893. LEBER.—B. d. o. G., 1897. SCHIECK.—Internat. Cong., Utrecht, 1899: v. Hippel's Festschrift. Halle, 1900. * BEST.—B. z. A., xliii, 1900. MANZUTTO.—B. z. A., xliv, 1900. TREACHER COLLINS.—Lancet, 1900.

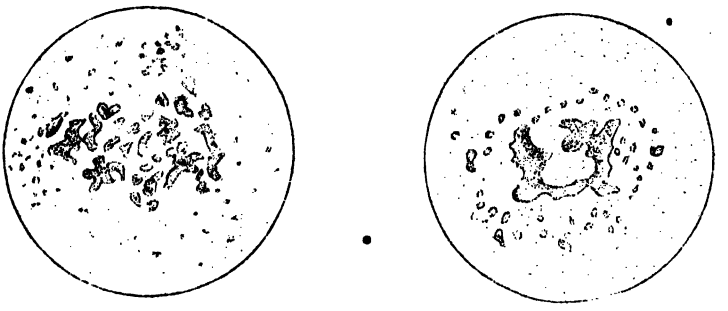
NODULAR OPACITY

Nodular opacity of the cornea (*knotchenförmige Hornhauttrübung*) was described by Groenouw, and has been more recently investigated by Fuchs. Raised grey spots are scattered over the cornea, usually smaller at the periphery and larger near the centre, where they may run together to form irregular opaque patches (Figs. 167, 168). The disease is probably due to some general agent, since it always affects both eyes, develops very slowly, requiring many years for completion, and sometimes occurs in several members of the same family. Similar

cases have been described by Chevallereau (*kératite goutteuse*) and Treacher Collins. The condition is allied to the reticular opacity (q. v.).

Microscopically Chevallereau found deposits of crystals of sodium

FIG. 167. FIG. 168.



FIGS. 167, 168.—NODULAR OPACITY OF THE CORNEA.
Fuchs, T. O. S., xxii; *see also* A. f. O., liii.

urate in his case. Groenouw found hyaline deposits, staining deeply with eosin. Fuchs made an exhaustive examination of portions of the cornea removed from one of his cases with the corneal trephine. The changes were of four kinds, and were limited to the superficial layers. (1) The lamellæ for a maximal thickness of 0·06 mm. stained faintly (Fig. 169), especially with van Gieson. In places the lamellæ were swollen and more homogeneous, and the lymph-channels were dilated, oval, or rhombic. The corneal corpuscles and their nuclei were swollen here. Bowman's membrane was absent. There was therefore the

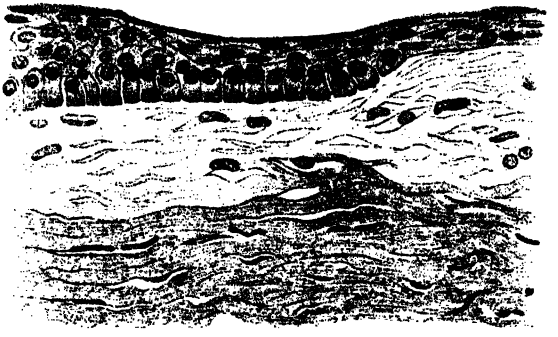


FIG. 169.—NODULAR OPACITY OF THE CORNEA.
Fuchs, T. O. S., xxii; *see also* A. f. O., liii.

picture of marked œdema in this situation. (2) In the altered superficial layers were raised spots corresponding with the larger grey opacities, having a maximum breadth of 0·5 mm. The lamellæ were

split up here into fine wavy fibres with spaces between them. The epithelium was slightly raised by the nodules, but this was partially counteracted by diminution in the number of layers, the cells of which showed the degenerative changes usual under such circumstances. (3) In places, especially where the changes were most advanced, amorphous masses lay between the swollen and the normal lamellæ. These contained broken up lamellæ and distorted nuclei. The amorphous material was finely granular, stained little with hæmatoxylin and eosin, yellow with van Gieson; it was probably coagulated fluid. It gave no definite mucin reaction with mucicarmin or thionin. (4) The superficial layers of the lamellæ, which were apparently normal when stained with hæmatoxylin and eosin or van Gieson, showed changes with other stains. They were coloured violet instead of blue by thionin; blue with Löffler's methylene blue when the normal ones were decolourised, and the same with Gram. The changes point to a mucoid degeneration which was lost in the later stages.

GROENOUW.—A. f. O., xlvi, 1, 1898. * FUCHS.—A. f. O., liii, 3, 1902. CHEVALLEREAU.—France médicale, 1891. TREACHER COLLINS.—T. O. S., xxii, 1902. FEHR.—C. f. A., xxviii, 1904.

RETICULAR OPACITY

Reticular opacity of the cornea has been described by Biber, Haab (*gitterige Keratitis*), and Dimmer; cases recorded by Treacher Collins and Block probably belong to this category. There is a lattice-work of fine raised lines in the superficial layers of the cornea; they are at first transparent, but become grey. The condition resembles nodular opacity in the chronic course of the disease and the occasional affection of members of the same family.

Dimmer examined a small portion of cornea removed from a case. The grey lines do not lie in the epithelium, but in the superficial layers of the substantia propria, and are probably due to folding of Bowman's membrane (Dimmer). Besides the fine lines there are minute grey punctate opacities, which project above the surface. These consist of a hyaline material, insoluble in alcohol, ether, and strong acids, and stained by eosin. There were needle-shaped crystals in the epithelium, which dissolved in mineral acids without giving off gas; they were probably triple phosphate (Dimmer).

BIBER.—Dissert., Zürich, 1890. HAAB.—Z. f. A., ii, 1890. DIMMER.—Z. f. A., ii, 1890. TREACHER COLLINS.—T. O. S., xix, 1899. BLOCK.—Niederl. ophth. Gesellschaft, 1899. FREUND.—A. f. O., xlii, 2, 1903.

PERIPHERAL SCLEROSIS AND ATROPHY

Peripheral sclerosis and atrophy of the cornea (*Randsclerose und Randatrophie der Hornhaut*) has recently been described by Fuchs. Only one case has yet been examined microscopically.

Most of the cases occurred in old people in connection with arcus senilis. A furrow forms spontaneously at the periphery of the cornea, without any ulceration having taken place (Fig. 170). It is situated between the arcus and the limbus, and may surround the cornea; it

may also occur in both eyes. The central wall of the depression is nearly perpendicular, the peripheral rises gradually; the floor is covered with epithelium, and is vascularised from the limbus vessels.

The eye which was examined was lost from glaucoma; there was no ectasia of the cornea. The gutter was 0·55 mm. broad; the floor was 0·57 mm. thick—about two-thirds the thickness of the cornea in the centre. Bowman's membrane ceased more than 2 mm. from the central edge of the furrow, and for about two-thirds of a mm. from the edge the lamellæ were broken up, wavy, and richly vascularised. The anterior half of the floor consisted of the same tissue, whilst the posterior half consisted of normal lamellæ. There was no evidence of round-cell infiltration or of any inflammatory process, and the loose tissue was

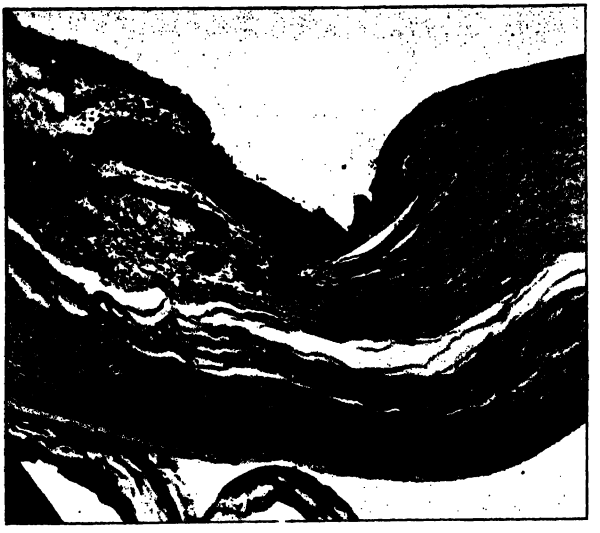


FIG. 170.—PERIPHERAL SCLEROSIS AND ATROPHY OF THE CORNEA. × 55.
From a specimen sent by Prof. Fuchs. This is evidently from the same specimen which is described by Fuchs, and figured in A. f. O., lii.

quite unlike a corneal cicatrix. The epithelium was thicker over the floor, owing to protection from pressure. The characteristic basal cells of the corneal epithelium reached only to the central steep wall; on the floor was conjunctival epithelium, distinguished by the much shorter cubical basal cells with deeply stained nuclei.

The condition is probably due to an advance of the conjunctiva into the cornea, brought about by some unknown stimulus. Bowman's membrane is destroyed, and the lamellæ are broken apart, fibrillated, and in large degree destroyed. The process is therefore much allied to that taking place in pterygium.

A somewhat similar condition, occurring in younger people, is mentioned by Fuchs, and is probably the same as Terrien's "dystrophie marginale." Schmidt-Rimpler's "chronic peripheral furrow keratitis

(*Furchenkeratitis*)" differs from peripheral sclerosis in that the furrow is central to the marginal opacity.

* FUCHS.—A. f. O., lii, 2, 1901. TERRIEN.—A. d'O., xx, 1900. SCHMIDT-RIMPLER.—Lehrbuch, 7th ed., p. 491.

PIGMENTATION

In rare cases of diffuse pigmentation of the conjunctiva the disease may extend on to the cornea. In two cases which I have seen there were tongue-shaped pigmented patches passing towards the centre of the cornea from the periphery. Microscopically the pigment consisted

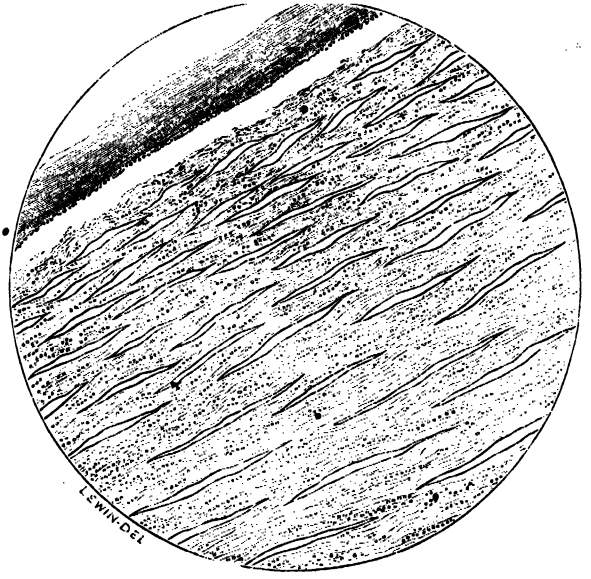


FIG. 171.—BLOOD-STAINING OF CORNEA.
Treacher Collins, T. O. S., xi.

of dense clumps situated in the epithelium, the substantia propria being normal. The pigment gave no iron reaction, and was bleached by the usual methods.

** YAMAGUCHI.—K. M. f. A., xlii, 1904.

Pigmentation of the cornea is usually due to blood-pigment or to deposits of foreign matter, *e.g.* metals, Indian ink, etc. Congenital opacities are occasionally coloured; they will be considered elsewhere.

Blood-staining.—The periphery of the cornea may become stained by blood after sub-conjunctival hæmorrhage in the vicinity. Pigmentation of the cornea as the result of hæmorrhage into the anterior chamber occurs with comparative rarity. It is interesting clinically in that the condition may be mistaken for dislocation of the lens into the anterior chamber. In many of the cases recorded the tension was raised, and it is probable that it is raised in the early

stages in all cases, and that this is an important factor in determining the transfusion of the cornea with blood. The whole cornea is at first stained; it gradually and very slowly clears from the periphery towards the centre. In one case it took twenty-five days to clear to the edge of the dilated (atropinised) pupil; a year after there was a grey patch, 4 mm. in diameter, in the centre of the cornea; in two and a quarter years the cornea was clear (Treacher Collins). The colour varies greatly, probably with the age of the staining; it is described as greenish black, greenish brown, greenish, rusty brown, reddish brown, etc. In all cases there is at first hyphæma. It may occur at any age. Its comparative rarity is probably due to the absence of tension at the

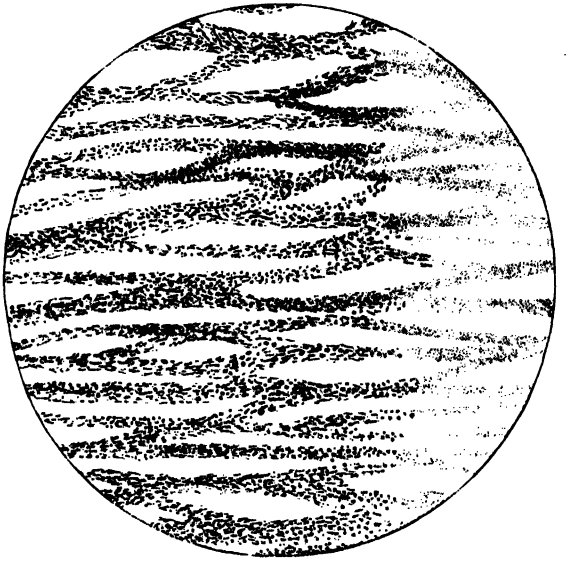


FIG. 172.—BLOOD-STAINING OF CORNEA.
Griffith, T. O. S., xiv.

onset of most hæmorrhages, the tension being sub-normal, owing to the presence of a wound.

The nature of the pigment has been the subject of much controversy. It doubtless varies with the age of the deposit, and is invariably a derivative of hæmoglobin. According to Treacher Collins, hæmatoidin is the chief constituent; but this is not always the case, since the deposit often gives the reactions for iron, and hæmatoidin contains no iron; also hæmatoidin is soluble in chloroform, whereas the granules are not always so (E. von Hippel). It is probable that the iron-containing pigment is hæmosiderin (Vossius); but doubtless other derivatives of hæmoglobin occur at various stages.

In some cases, but probably a minority, there is actual hæmorrhage into the cornea from new-formed vessels (Vossius, Scheffels), for corpuscles in various stages of degeneration have been observed. There can be no question that many of the cases occur without intra-

corneal hæmorrhage. In these the hæmoglobin of the broken down corpuscles in the anterior chamber is in solution, and filters through Descemet's membrane (Treacher Collins), or possibly enters the cornea through the spaces of Fontana (Weeks), but this is less probable.

It is natural that absorption should take place from the periphery, the site of the blood-vessels and most active lymph-flow. In cases in which new capillaries are present in the cornea the area surrounding them is free from granules (Baumgarten, Vossius), indicating the activity of absorption in this situation. The granules are extremely insoluble, and are probably removed by leucocytes.

The granules are usually present in vast numbers, are round, oval,

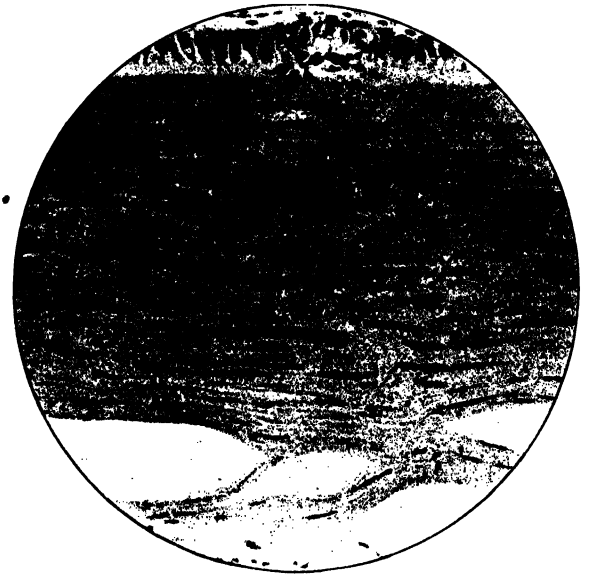


FIG. 173.—PIGMENT IN THE CORNEAL CORPUSCLES. × 180.

Vertical section. Slight œdema of the epithelium. Bowman's membrane is fibrillated and destroyed in one place by an aggregation of leucocytes. The corneal corpuscles are packed with dark granules.

or rod-shaped, highly refracting, and vary in size from 3 μ to 7 μ; they are therefore much smaller than red corpuscles (Figs. 171, 172). They are generally scattered throughout the corneal lamellæ, and are absent from the spaces. A few are present between the epithelium and Bowman's membrane, and in the spaces of Fontana.

These granules have naturally been regarded as the cause of the colouration by many observers (Lawford, Griffith, Treacher Collins, etc.). The absence of colour is somewhat against this idea, and the presence of distinct pigmented granules in the corneal corpuscles, noted by other observers (E. von Hippel), has led to their being regarded as the real cause. Indeed, the refractile granules may be entirely absent (Römer, Case iii). It can scarcely be doubted, however, that in

most of the cases they are the cause of the colouration. Their high refractility is itself sufficient to mask colouration when viewed by transmitted light.

Leber compared the granules to the fibrin deposits found by him in Aspergillus keratitis. This has been definitely disproved by Römer, who concludes that they are formed from the proteid constituent of hæmoglobin, which has further undergone hyaline degeneration. They do not stain with the ordinary fibrin stains, and they are, unlike fibrin, insoluble in a solution of neurin (Römer). Vossius regarded them as a hyaline degeneration of the corneal fibrillæ. Baumgarten showed that the apparent resemblance to micro-organisms was fallacious.

The granules are insoluble in alcohol, ether, and chloroform; they



FIG. 174.—PIGMENT IN THE CORNEAL CORPUSCLES. × 180.

Tangential section from the same specimen as Fig. 173. The corneal corpuscles are packed with round pigment granules. The darkly stained rod-shaped and broken up nuclei belong to infiltrating leucocytes.

are only slowly acted upon by strong acids and alkalies. They give no glycogen or amyloid reaction, and are unstained by van Gieson's solution, Weigert's elastic stain, etc. Nuclear stains (*e. g.* hæmatoxylin, alum and lithium carmin) do not stain them, nor aniline dyes, *e. g.* Bismarck brown, gentian violet, methylene blue. They are not stained by osmic acid. They are stained pink by eosin, or hæmatoxylin-carbol-fuchsin; red by hæmatoxylin-saffranin-picric acid. Intense over-staining with Weigert's fibrin stain colours them faintly (Römer). They are stained by iodine-green or methyl-green (Griffith).

I have seen an anomalous case in which, following a perforating wound with a splinter of steel, the cornea and other parts of the eye were intensely pigmented. No foreign body was found on examination,

but there was considerable intra-ocular hæmorrhage. The pigment granules were confined to the corneal corpuscles (Figs. 173, 174). They gave a well-marked iron reaction.

BAUMGARTEN.—A. f. O., xxix, 3, 1883. LAWFORD.—T. O. S., viii, 1888. VOSSIUS.—A. f. O., xxxv, 2, 1889. LEBER.—A. f. O., xxxv, 1 and 2, 1889. * TREACHER COLLINS.—T. O. S., xi, 1891; xv, 1896. WEEKS.—New York Eye and Ear Infirmary Rep., 1893. GRIFFITH.—T. O. S., xiv, 1894. HIRSCHBERG.—C. f. A., xx, 1896. E. v. HIPPEL.—A. f. O., xliv, 3, 1897. * RÖMER.—Vossius' Sammlung, ii, 8, 1899. SCHEFFELS.—Z. f. A., v. 1901.

Metals.—Deposits of lead, iron, silver, copper, etc., have been described in the cornea as the result of treatment or accident. In argyrosis Knies found intense staining of Descemet's membrane with silver, whilst the other parts of the cornea were normal. This might be anticipated from the affinity shown by silver for elastic fibres (*v.* p. 110). Deposits of lead upon ulcers treated with Lotio plumbi are quite superficial. Iron staining will be described elsewhere in treating of siderosis bulbi. The other stains are rarities which have been observed only clinically.

KNIES.—K. M. f. A., xviii, 1880.

Tattooing.—The deposits of pigment in leucomata after tattooing were first examined by Hirschberg, whose results I can confirm. The black pigment forms spindle-shaped or irregular lumps between the fibres of the scar tissue. It is mostly free, but granules are found in some of the cells, probably in process of removal, and also in the walls and lumina of vessels. Only the deepest layers of the epithelium ever contain pigment.

HIRSCHBERG.—A. f. O., xxviii, 1, 1882.

CYSTS

Cysts of the cornea are rare; they are mostly *implantation cysts*, due to injuries or operations, whereby particles of the superficial epithelium are carried into the stroma. The displaced epithelium then proliferates, forming a mass like the cholesteatomata, or pearl tumours of the iris. The central cells break down and disappear, fluid collects, and a cyst is formed in the substance of the cornea, lined by stratified epithelium. Such cases have been described by Treacher Collins. One followed a perforating wound with a shot; another occurred in a shrunken eye from which a cataract had been extracted (Fig. 175); a third was a large cyst following a perforating wound with a stick (Figs. 176, 177). The epithelium is usually irregular and ill developed; the number of layers varies in different parts, the outer ones consisting of cubical and the inner of flattened cells. The cavity often contains granular or hyaline material, and there are often patches of epithelium without any cavity. The corneal tissue around is generally infiltrated and vascularised, and the fibrous tissue is especially dense immediately around the cysts.

The possibility of direct continuity with the superficial epithelium in these cases can only be eliminated by serial sections. It is not uncommon after cataract extractions, usually in eyes which have later

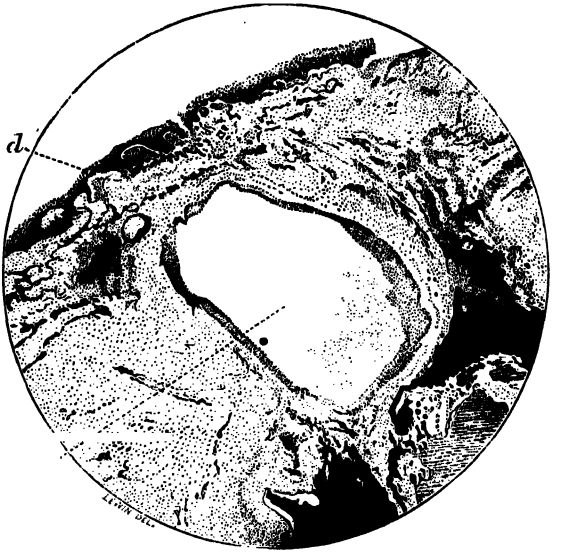


FIG. 175.—CYST OF CORNEA.

From Treacher Collins. Epithelial cyst in cornea of a shrunken eye, after cataract extraction. *d*, Bowman's membrane; *c*, cyst. (R. L. O. H. Rep., xiii.)

become glaucomatous, to find that the epithelium has grown down into the cornea or sclera, and even into the anterior chamber. The track is often very irregular and tortuous, so that islets of epithelium are seen in sections. There may be a devious fistulous track in these cases, in spite of which the anterior chamber is maintained, the tortuosity allowing the walls to be kept in contact in places by the intra-ocular tension (*v.* p. 165).

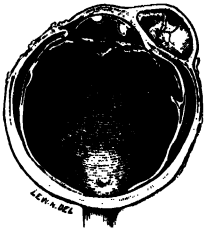


FIG. 176.—CYST OF CORNEA.

From Treacher Collins. Epithelial cyst following wound with a piece of wood. (T. O. S., xii.)

Cystic spaces may also occur with uveal pigment in the walls. In these there has probably been prolapse of iris, which has been treated. Alt describes four cases, in two of which the cysts were lined by uveal pigment; another had perfectly smooth walls; and the fourth had trabeculæ passing from one side to the other. There is no mention of an epithelial lining.

Small cysts in the epithelium (vesicular or bullous keratitis) are common (*v.* p. 176).

Spurious cysts also occur, which are found on microscopical examination to consist of masses of loose, œdematous (? myxomatous), fibrous tissue (Treacher Collins).

True lymphatic *retention cysts* are of great rarity. One such has been described by Ginsberg in a chick. It had no continuous cellular lining,

but only an incomplete layer of flat connective-tissue cells. It probably arose by distension of the lymphatic channels, and absorption of some of the lamellæ. Another case has been recorded by Just, but without microscopic examination.

There is a small group of cases in which cysts have developed in conjunctiva laying *on* the cornea. There has usually been previous injury or blenorrhœa, and the condition is probably due to the formation of an extensive pseudo-pterygium by the adhesion of the chemosed conjunctiva to the corneal wound or ulcer. The simplest expression of the condition is found in a case of Reid's, reported by Bietti. Here the conjunctival epithelium was fused to the corneal at some distance from the limbus. In this manner an epithelial cyst was formed, bounded by conjunctiva in front and cornea behind. In Bietti's own case the union was more intimate. There was a single cyst with a small diverticulum, lined by stratified epithelium of varying thickness. Bowman's membrane was destroyed under and around the cyst, and the corneal

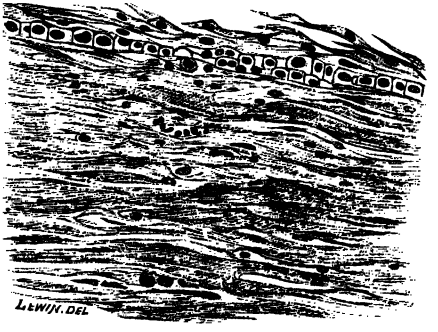


FIG. 177.—CYST OF CORNEA.
From Treacher Collins. Showing laminated epithelium of the cyst in Fig. 176.

lamellæ were sclerosed and infiltrated. The condition is ascribed to a pseudo-pterygium following superficial marginal keratitis. In Schieck's case there was a trilocular cyst following a perforating ulcer with prolapse of iris. Reis reports a similar case, with several cysts. They were all lined with stratified epithelium and lay principally in conjunctival tissue, the cornea forming a posterior basis.

Czermak describes cystic spaces in corneal scars; in all the cases the iris was involved, a triangular space passing along the iris from the anterior chamber towards the cyst without directly communicating with it.

Gruening reports an extraordinarily large cyst developed between the layers of the cornea and sclerotic at the limbus, in a girl of fourteen, after an iridectomy (*cf.* Fig. 176). It communicated with the posterior chamber by two minute canals, and was lined irregularly by a thin layer of endothelium.

Tertsch reports a cyst of the posterior part of the cornea in a buphthalmic eye. Descemet's membrane was separated from the corneal lamellæ, and formed a space which communicated with the ante-

rior chamber through a tear in the membrane. The cyst was lined with endothelium, continuous with that on the back of the cornea. Descemet's membrane was also ruptured in other places.

* TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1, 1890; T. O. S., xii, 1892. ALT.—A. of O. and Otology, vi, 1878. GINSBERG.—C. f. A., xxi, 1897. JUST.—Ann. d'Oc., lxx, 1873. BIETTI.—K. M. f. A., xxxviii, 1900. SCHIECK.—A. f. O., lii, 2, 1901. REIS.—K. M. f. A., xl, 1902. CZERMAK.—A. f. O., xxxvi, 2, 1890. GRUENING.—T. Am. O. S., 1901. * TERTSCH.—A. f. O., lvi, 2, 1903.

TUMOURS

PAPILLOMA AND CORNEAL "HORN"

Bowman described a "warty condition" of the cornea; this refers to epidermoid epithelium over a hyperplastic scar. The first true papilloma was described by Gayet in 1879. It occurred in a man of sixty-seven, and involved nearly the whole of the cornea. It consisted of papillæ, which occupied the position of Bowman's membrane, and were covered by corneal epithelium. It probably started at the limbus and invaded the cornea. This is also true of Ayres' case.

Baas reported a "corneal horn," which consisted of a papilla covered by horny epithelium.

Demicheri's tumour occupied the upper and inner half of the cornea, and also probably began in the limbus. The fibrous tissue was slight and poor in vessels.



FIG. 178.—"CORNEAL HORN." Lawson, T. O. S., xx.

In Lagrange's case there was a large cauliflower-like growth, the pedicle of which was exactly circumscribed by the limbus. It was a typical papilloma. Bowman's membrane was destroyed, but some of the deeper layers of the cornea were intact, and the eye was otherwise healthy.

Arnold Lawson has published a case of "cicatrix horn" growing from the cornea (Fig. 178). It was conical in shape, five-eighths of an inch in length, and an inch and a half round the base. It grew from an anterior staphyloma, and consisted of an outer layer of fibrillated material, staining badly, and an inner layer occupying three-quarters of the section, composed of small, round, nucleated cells. It can hardly be doubted that this is no true new growth, but merely a mass of granulation tissue which was unusually exuberant. Projecting between the lids, the surface became dry, and the detritus was not cast off by movements of the lids, etc., owing to the marasmic condition of the child.

BOWMAN.—Lectures, London, 1849. GAYET.—Lyon médical., 1879. AYRES.—Jl. of the Amer. Med. Assoc., 1891; Ophth. Rev., x, 1891. BAAS.—Ziegler's Beiträge, xx. DEMICHERI.—A. d'O., xix, 1899. * LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. ARNOLD LAWSON.—T. O. S., xx, 1900.

Fibroma

Many of the cases described as fibromata of the cornea are merely hyperplastic scars. To this group belong those described by Pagenstecher and Genth, Scott and Story, Silex, Zirm, Vossius, Westcott, and others. These occurred respectively in an old scar, in trachoma, in an adherent leucoma, etc. They were either localised swellings or diffuse, and differed in no respect from ordinary pseudo-corneæ, except in the overgrowth of vascular connective tissue.

A case described by Reishaus, belonging to the same group, offers some peculiarities. It occurred in a woman of forty-six, who had suffered for years from chronic conjunctivitis with papillary hypertrophy. The swelling had existed for two years or more; it was hard, reddish, and covered the lower half of the lower corneal quadrant. It was cured by excision, the base being cauterised. It consisted of laminated connective tissue, rich in cells, especially near the vessels. There were no tubercle bacilli. There were numerous mast-cells, and also many small round globules, about the size of red corpuscles, which stained with aniline dyes; red with fuchsin. These were regarded by the author as blastomycetes; they stained bright red with Busse's specific stain.

These "fuchsinophile" bodies are common in chronically inflamed tissues, and are probably only hyaline bodies. (On the subject of blastomycetes in relation to the eye, *see* Stoewer.[1])

Capellini has reviewed the published cases of corneal fibroma, and added two others, one of which he calls a true fibroma, as opposed to a hyperplastic scar, and the other, on account of its extreme vascularity, a telangiectatic angio-fibroma. Both seem to me to be more probably types of hyperplastic scars (pseudo-corneæ), which are by no means infrequently met with.

There are, however, other cases which are apparently true fibromata of the cornea, such as those described by Quaglino and Guaita, Falchi, Benson, Gallenga, Rogman. Some of these were pedunculated and polypoid, growing from the centre of the cornea. They are usually covered with epithelium, which resembles "corneal" epithelium, but may have mucous cells or be horny on the surface. The growth itself consists of irregular bands of fibrous tissue with scanty flat and round cells. More rarely the bundles are laminated, and in Rogman's case the growth consisted of embryonic spindle-shaped cells.

The ages of the cases cited were 48, 28, 19, and 72, 4, and 30; three were men and three women.

Pagenstecher and Genth.—Atlas, Plate xvi, Wiesbaden, 1875. Scott and Story.—Ophth. Rev., 1888. Silex.—K. M. f. A., xxvi, 1888. Zirm.—A. f. O., xxxvii, 3, 1891. Vossius.—B. d. o. G., 1895. Westcott.—Ann. of Ophth., 1897. Reishaus.—B. z. A., xxxi, 1898. Capellini.—K. M. f. A., xxxix, 1901. Quaglino and Guaita.—Ann. di Ott., xiii, 1879. Falchi.—Ann. di Ott., xiv, 1885. Benson.—Ophth. Rev., 1887; T. O. S., x, 1890. Gallenga.—Arch. di Ott., iii, 1896. Rogman.—Ann. d'Oc., cxxv, 1901.
* Lagrange.—Tumeurs de l'Œil, Paris, i, 1901.

[1] Stoewer, A. f. O., xlviii, 1, 1899.

Myxoma

Adler, in 1871, reported the case of a "myxoma" of the otherwise normal cornea in a young man of nineteen. It was examined by Wedl; it consisted of fibrous tissue with numerous cystic spaces, and was covered with epithelium.

Another case was published by Mitvalsky, of a woman, æt. 26, with a polypoid growth from the centre of the cornea. The eye was blind from scrofulous keratitis in infancy; it had become staphylomatous, and had been operated on by simple ablation. The tumour was as large as a cherry, and the stalk was 4 mm. in diameter. It had been growing for two years. The surface was smooth and glistening. The epithelium resembled that of the cornea; the parenchyma consisted of typical myxomatous tissue with large cystic spaces, the older ones being surrounded by more compact tissue.

Barrett, in 1888, reported a double congenital tumour of the cornea and sclera as a myxo-fibroma, but the diagnosis is doubtful.

Simon described a myxo-fibroma in a man æt. 61. The cornea had ulcerated six years before, after a lime burn, and had been treated by Saemisch's section. The eye was painful, and was enucleated. The tumour, 9 mm. long by 3·5 mm. thick, was surrounded by corneal tissue both at the periphery and below. It was covered by epithelium, which was thickened so that there were thirty layers in places. The parenchyma consisted of dense cellular fibrous tissue with many blood-vessels. On the nasal side there was a small elevation, in which the fibrous tissue was replaced by stellate and round-cells embedded in a homogeneous matrix. On the temporal side there was a hyaline membrane under the corneal tissue, derived probably from the endothelial cells of Descemet's membrane.

Simon regarded this tumour as a "scar-fibroma" (Narbenfibrom) which had undergone myxomatous degeneration; and this is probably the explanation of all these myxomata.

Whether they are true myxomata, containing mucin, or merely œdematous connective-tissue growths has not been settled by crucial chemical tests.

Adler.—Wiener med. Woch., 1871. Mitvalsky.—A. d'O., xiv, 1894. Barrett.—Australian Med. Jl., 1888. Simon.—C. f. A., xvi, 1892.

Teratoid Tumours

Dermoid and teratoid tumours which are strictly limited to the cornea are of extreme rarity. It may almost be doubted whether they occur at all.

Fuchs described a dermoid in a boy of twelve, occupying the outer half of the right cornea, extending from the centre to the limbus, but not beyond this. It consisted chiefly of dilated lymphatics lying in connective tissue. The epithelium covering it was corneal, not epidermal. The

growth contained no hairs or sebaceous glands, but there was a large acinotubular gland resembling Krause's glands.

Bernheimer reported an extraordinary case in a child six months old. There was an anterior staphyloma, almost certainly due to intra-uterine perforating ulcer. The pseudo-cornea was greatly thickened, the anterior part forming a dermoid tumour. The epithelium was unequally thickened, horny on the surface, and showed many down-growths. There were many hairs, with hair-follicles and sebaceous glands. The ground tissue consisted of dense connective tissue, containing capillaries, and fine bands and groups of round-cells. At the periphery the fibrous tissue was looser, and contained masses of adipose tissue. Descemet's membrane was intact except at one spot, where it was broken and the ends were curled up. Adherent to it was the atrophic iris, with its retinal pigment layer.

The tumour described by Cohn was of the teratoid type. The epithelium was like that of the conjunctiva, possessing goblet-cells and no horny layer, except at the periphery. Here there were no papillæ, but these were present in the centre. The connective tissue contained many glands resembling Krause's, but apparently secreting mucus which stained with thionin. There were also islands of cartilage and fat, as well as many vessels and lymphocytes. The lamellæ were mostly replaced by young connective tissue. There were several breaks in Descemet's membrane, with anterior synechiæ.

Fuchs.—K. M. f. A., xviii, 1880. Bernheimer.—A. f. A., xviii, 1887. Cohn.—Inaug. Diss., Heidelberg, 1896.

Sarcoma and Endothelioma

Sarcoma of the cornea proper is extremely rare.

Rumschewitsch describes a case in a man æt. 61, who had lost the sight of his eye after a blow upon the head. The tumour was mushroom shaped, the pedicle springing from the cornea, and having no conection with the conjunctiva; it was 7·5 mm. thick. Bowman's membrane was intact up to the pedicle. The corneal lamellæ passed into the connective-tissue strands of the pedicle, which contained many blood-vessels. The tumour itself was very vascular, with hæmorrhages. The cells were chiefly spindle shaped, with very little intercellular substance, but there were many round-cells, which were indistinguishable from leucocytes, and were chiefly aggregated near the capillaries. The growth was covered by epithelium, which was broken in places by hæmorrhages.

Blanquinque describes a melano-sarcoma in a woman æt. 60, which had been noticed first twenty years previously as a red spot near the centre of the cornea; it had been increasing for nine years, extending up and out to 1 mm. from the limbus. It was the size of a pea, greyish, smooth, not ulcerated, firm, painless. The tumour was shaved off by a Graefe knife. It was examined by Malassez. It was lobulated, covered with epithelium, some of the deeper cells of which were pigmented. The main mass consisted of cells which were very variable in size and

shape, some grouped in spherical masses. The nuclei were masked by small yellowish-brown "granulations." There were very few vessels and no hæmorrhages.

Chantinière reported a man æt. 33, from whom a small tumour was removed; it recurred rapidly. It was covered by normal epithelium and Bowman's membrane, which was perforated at several places. Angular cells of connective-tissue origin infiltrated the anterior layers of the substantia propria and passed through the holes in Bowman's membrane. There were very few vessels, derived from a leash from the conjunctiva.

The case of Donaldson, examined by Treacher Collins, extended over the sclerotic for 4 mm., and is therefore a doubtful case. It was



FIG. 179.—ALVEOLAR SARCOMA OF CORNEA. × 100.
Donaldson and Treacher Collins, T. O. S., xv.

made up of groups of round-cells, surrounded by fibrous tissue and elongated cells, and was diagnosed as an alveolar sarcoma (Fig. 179).

Gonin reports the case of a man, æt. 32, with a melanotic (?) sarcoma of the cornea of two months' growth. It was removed, after iridectomy, by a Graefe knife, and the base cauterised. There was no recurrence sixteen months later. It consisted of fusiform cells of medium size, with little intercellular substance; there were patches of degeneration, and signs of alveolation. The pigmentation was probably due to hæmorrhage, as the growth had been previously incised; moreover scattered hæmorrhages were present. The pigment did not give any reaction for iron.

Rogman relates the case of a woman of sixty-five with the appearance of a small prolapsed iris. On removal it was found to consist of round

and spindle-shaped cells, with signs of an alveolar arrangement; some were densely pigmented.

Rumschewitsch's second case occurred in a girl, æt. 14, with advanced trachoma, and was doubtless pannus with an unusual degree of hyperplasia.

v. Michel records metastatic deposits of melanotic sarcoma in the cornea, accompanying an episcleral growth.

Fumagalli records a primary sarcoma in a woman of fifty-two, whose cornea was injured by a finger-nail seven years before. It had the structure of a perivascular sarcoma, growing from new-formed blood-vessels.

None of these cases are above suspicion as to diagnosis. The evascular fibrous stroma of the cornea, like tendons and aponeuroses, might be expected to enjoy relative immunity from malignant growths, whilst it is always impossible to exclude invasion from the periphery,

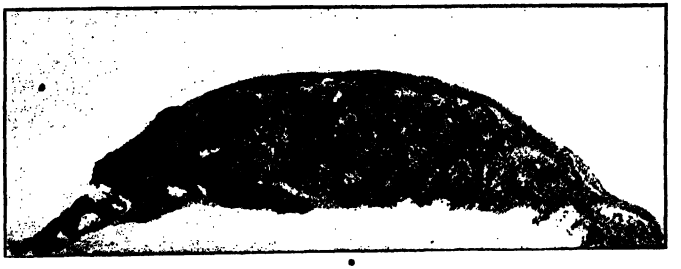


FIG. 180.—ENDOTHELIOMA OF THE CORNEA. × 12.

Slowly growing, frequently recurrent growth of cornea, in an adult (*see* T. O. S., xxiii, 1903, Sinclair and Parsons). Note the alveolar arrangement.

from which the blood-supply must necessarily be derived. The resemblance of embryonic connective tissue in inflammatory granulations to sarcoma and the loss of the iron reaction in old hæmorrhagic pigmentation form insuperable barriers to certitude of diagnosis in the present state of knowledge. Nevertheless malignant proliferation of the fixed corneal corpuscles cannot be definitely eliminated. Should it occur, the disposition of the corneal lamellæ might be expected to give rise to a quasi-alveolar arrangement.

Donaldson's and Fumagalli's cases most nearly resemble the one which I have described as an endothelioma of the cornea. Transverse sections of the growth were plano-convex (Fig. 180). The convex surface was covered with epithelium, which was flattened, varied greatly in thickness, and was absent near the periphery on one side. The growth consisted of masses of epithelioid cells arranged in an alveolar manner, enclosed in capsules of spindle-celled fibrous tissue (Fig. 181). This tissue stained red with van Gieson, and fibrillæ passed between the outer cells of the masses, but the larger central parts were devoid of any definite intercellular stroma.

The epithelioid cells varied greatly in size and shape; many showed

karyokinetic phases, others atypical nuclear changes. The aggregations also varied in size. They were mostly oval, and the smaller ones invaded the epithelium in places, recalling the conditions found in congenital nævi (*v.* p. 127).

There can be little doubt that this growth was an endothelioma, and that it originated in the limbus, and is not a true autochthonous corneal growth. There are faint indications of *débris* of red corpuscles in a few



FIG. 181.—ENDOTHELIOMA OF THE CORNEA. × 120.
From the same specimen as Fig. 180.

of the alveoli, and this points to blood-vascular endothelium as the origin of the cells.

RUMSCHEWITSCH.—A. f. A., xxiii, 1891. BLANQUINQUE.—Rec. d'O., 1892. CHATINIÈRE. —*See* LAGRANGE. DONALDSON.—T. O. S., xv, 1895. GONIN.—Ziegler's Beiträge, xxiv, 1898. ROGMAN.—Ann. d'Oc., 1901. RUMSCHEWITSCH.—A. f. A., xxxi, 1893. v. MICHEL.—Beitr. z. Onkol. d. Auges., Würzburg, 1899. FUMAGALLI.—La Clin. Oc., 1902; K. M. f. A., xl, 1902. * SINCLAIR AND PARSONS.—T. O. S., xxiii, 1903. * LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901.

EPITHELIOMA

Most of the cases of so-called epithelioma of the cornea are really growths starting in the limbus at the site where the conjunctival epithelium changes into corneal. Such sites form the commonest places at which epitheliomata develop in the body, *e.g.* the edge of the lid, lip, anus, etc. To this group belong the cases of Adams, Colsman, Goldzieher, Manfredi, Manz, and others. I have examined the sections of the case described by Lawford, and there can be no doubt that this was a case of Mooren's ulcer, and therefore not an ordinary epithelioma.

Cases of primary epithelioma of the cornea itself are excessively rare. Only six cases can be found in the literature in which the accuracy of the diagnosis is probable.

A patient of Galezowski's had a small growth in the centre of the cornea, which was removed, and examined by Ranvier and Cornil, who reported that it was a carcinoma, limited to the superficial layers, leaving the substantia propria quite healthy.

Dolgenkow describes a large, hard, pale red, lobulated tumour of the cornea, which developed during eighteen months. It was mushroom shaped, the pedicle being short and thick, and growing only from the cornea. The sclera and conjunctiva were normal apart from round-celled infiltration.

Sgrosso describes the microscopical features of two small tumours shaved off from the cornea. The first was separated 1 mm. from the limbus; it consisted of polygonal cells with large nuclei, forming cones which penetrated into the substantia propria, Bowman's membrane being destroyed. The whole of the tumour was removed. In the second case, the epithelium had proliferated downwards slightly into masses of granulation tissue, which replaced Bowman's membrane; the lamellæ were intact. The drawing gives the impression that there was a distinct basement membrane, the growth being probably a benign hyperplasia.

Snellen Jr. reports the case of an elderly man who had been in the East Indies, who developed a true corneal epithelioma in connection with a pterygium. This is the best example of an epithelioma, but its association with a pterygium throws some doubt on its corneal origin. It invaded the substantia propria, extending under Bowman's membrane and the superficial epithelium, both of which were intact over the greater area of the cornea. It did not invade the anterior chamber or the sclerotic, and such changes as were present in the uveal tract and retina were inflammatory. There can be no doubt about the epitheliomatous nature of the growth.

Nuel refers to a similar case in an East Indian, and to another of Steiner's, but gives no details.

Alfieri's case is the most fully reported. The growth developed in the centre of the cornea, and had no communication with the limbus. It occurred in a man, æt. 70, who had been struck in the right eye by a branch twenty years before; the cornea became opaque. A few months before being seen a red excrescence appeared upon the scar, finely lobulated, umbilicated, and separated from the limbus by a ring of opaque cornea. The eye was enucleated, and the growth found to consist of epithelial cells, flattened near the surface, rounder and more cubical in the deeper layers. The central depression was probably due to necrosis.

Aubineau observed a corneal tumour in a man æt. 65. It was white, flat (2—3 mm. thick), in the lower and outer part of the cornea, quite separated from the limbus. It was described as an "epithéliome lobulé corné et muqueux."

The cases, therefore, of true corneal epitheliomata are extremely rare, and are all open to more or less doubt. It seems probable, however, that the corneal epithelium is capable of malignant proliferation,

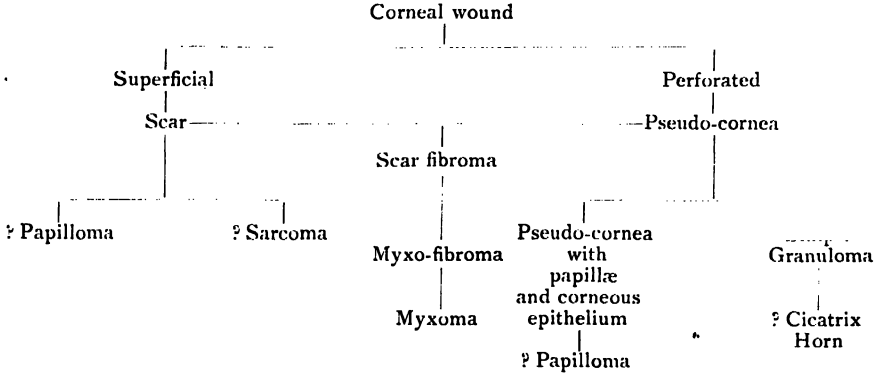
and that it has but slight tendency to extend deeply (Lagrange). It is rare for epibulbar growths to invade the interior of the eye; epithelioma of the cornea apparently never does. The substantia propria offers some resistance to the invasion, setting up a barrier of embryonic connective tissue around the epithelial cells. The fact that the canal of Schlemm and the anterior perforating vessels lie under the conjunctiva accounts for the fact that the growth never becomes intra-bulbar; added to this is the fact of the intra-ocular pressure which prevents the growth from bursting through elsewhere. Like all tumours, they grow in the direction of least resistance, which in this case is forwards and peripherally.

It is extremely noteworthy that no epithelioma of the uninjured cornea has ever been observed.

ADAMS.—T. O. S., ii, 1882. COLSMAN.—K. M. f. A., vii, 1869. GOLDZIEHER.—In Nagel's Jahresb., 1875. MANFREDI.—Riv. Clin., 1870. MANZ.—A. f. O., xvii, 2, 1871. LAWFORD.—R. L. O. H. Rep., xii, 3, 1889. GALEZOWSKI.—Traité des Maladies des Yeux, i, p. 312, 1870. DOLGENKOW.—West. Opht., 1885 (*see* LAGRANGE). SGROSSO.—Ann. di Ott., xxi, 1892. SNELLEN, JR.—6me Sess. semestrielle d'Opht., Utrecht, 1894. NUEL.—In NORRIS AND OLIVER'S System, iv, London, 1900. ALFIERI.—Arch. di Ott., v. AUBINEAU.—Soc. d'Opht. de Paris, 1898; in Nagel's Jahresb., 1898. * LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. BAAS.—Z. f. A., x, 1903.

GENERAL REMARKS UPON CORNEAL TUMOURS

A review of the recorded cases of corneal tumours leaves one in great doubt as to their true status. No sharp line can be drawn between purely inflammatory conditions and many so-called growths. There is an even gradation from the simple corneal scar to the myxoma on the one hand and the papilloma on the other, the horn occupying an intermediate position. This may be diagrammatically represented thus—



Whether the true papillomata invariably develop thus or may arise *de novo* must be left to future research to decide. And further, whether any of these conditions are truly corneal in origin is open to doubt. Even inflammation in the absence of blood-vessels is unknown, and only epithelium is capable of repair without their agency, direct or indirect.

The same applies with equal force to the new growths, both benign and malignant, for all are vascular, though in varying degree, and derive their vessels from the limbus. Most doubtful of all are the malignant growths, especially the epitheliomata and the endothelial type of sarcomata. The proclivity of the former to arise at sites where the epithelium changes in character is well known, though their occurrence elsewhere is an established fact. As regards the endotheliomata, there are no vessels in the cornea, and the only endothelium is around the nerves. The endothelioma of the cornea which I have described undoubtedly originated in the limbus, and the case would seem to be unique. As to the embryonic spindle-celled type of sarcoma, it may be doubted whether some of them are not simple granulomata (granulation tissue).

CHAPTER IV

THE SCLEROTIC

THE NORMAL SCLEROTIC

THE sclerotic is the main supporting envelope of the eye. It is thickest at the posterior part, especially around the optic nerve (1·0—1·2 mm.); and thinnest at the equator, where it is covered by the muscles (0·3 mm.). More anteriorly it is reinforced by the expansions of the tendons of the recti and again becomes rather thicker (0·4—0·5 mm.).

As mentioned before, it overlaps the cornea like the rim of a watch-glass. Just behind this it is thinned by an internal furrow, *sulcus scleræ internus* (Schwalbe), which is spanned by the *ligamentum pectinatum iridis*, and has the canal of Schlemm at its apex.

The sclerotic consists of fibrils of connective tissue united into bundles, resembling the lamellæ of the cornea, but less regular and closer packed. The bundles run chiefly in two directions, meridionally, *i. e.* from before backwards, and equatorially, *i. e.* concentric with the margin of the cornea. But there are also many oblique bundles, and the arrangement is much interrupted by the entrance of the tendons of the recti and the obliques. Thus in front of the equator most of the superficial bundles are meridional, the deep equatorial; the superficial and middle ones run into the cornea; the anterior bundles are finer, firmer, and more closely plaited. The recti tendons reinforce the meridional fibres. Between the muscles, the external bundles are mostly equatorial, the internal meridional. The posterior calotte is more complex, more of the fibres being oblique, and fewer equatorial. The oblique tendons further reinforce the oblique and meridional fibres (Ischreyt).

Mingled with the white connective-tissue fibrils are an immense number of extremely fine elastic ones, the general arrangement of which can be traced by special stains (acid orcein or Weigert's elastic-tissue stain) (Sattler, Treacher Collins, Ischreyt, and others). These are fewer in youth. They run for the most part as wavy fibrils in the same direction as the white fibres. At the limbus they circle round the cornea, so that they appear as minute dots in antero-posterior sections. The outer layers contain more elastic fibres than the inner, and they are more numerous posteriorly than anteriorly (Treacher Collins). According to Ischreyt, they increase from without inwards posteriorly, whilst at the equator they are richest on the surface, rather less marked in the inner layer, and scanty in the middle layers. They form a ring around

Schlemm's canal, and are cut transversely here in meridional sections. They also form a ring around the optic nerve, and the lamina cribrosa is full of them, though they are absent here in the fœtus (Kiribuchi).

Posteriorly the outer layers of the sclerotic are continuous with the dural sheath of the optic nerve, whilst many of the inner layers, including a particularly large number of elastic fibres, are carried across the nerve as it lies in the foramen scleræ, and form the lamina cribrosa.

Between the bundles of fibres are lymph-spaces, containing fixed connective-tissue cells, though these are far less numerous than in the cornea. There are not infrequently scattered pigment-cells, especially in the inner layers, and others often accompany the perforating vessels and nerves. Occasionally patches of pigment occur (melanosis scleræ, Hirschberg). These are commonest in the episcleral tissue (*cf.* Treacher Collins), but are also found in the true sclera, thus approximating the condition often found in lower animals. They are usually associated with abnormally dark pigmentation of the uveal tract, the disc, and other parts of the body, as well as with pigmented moles.

The inner surface of the sclerotic is normally pigmented, and forms the *lamina fusca*. It is united by fibrils of pigmented connective tissue with the choroid, and is lined by endothelial cells, forming the external wall of the supra-choroidal lymph-space. The outer surface of the sclerotic is also covered with a single layer of endothelial cells, forming the ocular wall of Tenon's capsule. The endothelial covering is reflected over all the vessels, nerves, and muscles which pass across the space. Thus they all invaginate the space, and never actually enter it.

The proper blood-vessels and nerves of the sclerotic are few in number. Arteries are given off from the short posterior and the anterior ciliaries. The posterior ciliary veins—smaller than the corresponding arteries—are derived entirely from the sclerotic; the anterior ciliary veins are only in part derived from the sclerotic. Branches of the posterior ciliary arteries anastomose with branches of the central retinal vessels, and form an anastomotic ring, situated in the sclerotic around the optic nerve (*Circulus arteriosus* of Zinn). This is important as being an indirect anastomosis between the choroidal and retinal circulations (*see* Parsons). Some of the equatorial scleral veins open into the venæ vorticosæ. A scanty nerve-supply is derived from the posterior ciliary nerves, as they run between the sclerotic and choroid. Their ultimate distribution has been investigated by the Golgi method by Bach.

SATTLER.—B. d. o. G., 1896, 1897. TREACHER COLLINS.—R. L. O. H. Rep., xv, 1899. ISCHREYT.—A. f. O., xlviii, 3, 1899; A. f. O., xlix, 3, 1900; K. M. f. A., xl, 1902. BIETTI—Arch. di Ott., iv, 1897; A. f. A., xxxix, 1899. HIRSCHBERG.—A. f. O., xxix, 1, 1883. STUTZER.—A. f. O., xlv, 2, 1898. KIRIBUCHI.—A. f. A., xxxviii, 1899. PROKOPENKO.—A. f. O., lv, 1, 1902. TREACHER COLLINS.—T. O. S., xiv, 1894. PARSONS.—The Ocular Circulation, London, 1903. BACH.—A. f. A., xxxiii, 1896.

WOUNDS AND INJURIES

Most injuries of the sclerotic are perforating wounds and ruptures. In all these cases the injury is complicated by wounding of the con-

junctiva, episclera, uveal tract, and retina in varying degree. Ruptures may indeed be subconjunctival, but wounds invariably injure the conjunctiva and episclera if from without, or the retina and choroid if from within. Hence in all cases some highly vascular tissue is affected in conjunction with the sclerotic. This is of the utmost importance, since it has been found by pathological observation and by experiment that repair takes place almost entirely through the agency of these vascular tunics. This was indicated even in the earliest experiments by Ljubinsky (1867). Roth thought the cells were derived from the vitreous and sclerotic, the retina and choroid being inactive. Miyshita ascribed the healing of a scleral wound to the sclerotic alone, Baquis to sclerotic and episclera. Tepljaschin agreed in the main with Ljubinsky, but attributed a minor function to the vitreous and sclerotic.

More exhaustive and more recent experiments and observations have been carried out by Franke (1895), Krückmann (1896), Stoewer (1898), and myself (1901—2). Franke and Stoewer operated upon rabbits, the former examining wounds of a duration of four, eight, twelve, twenty-four hours, and every other day up to eighteen days. Krückmann paid most attention to the changes during the first twenty-four hours, but also continued the investigation up to 120 days; he experimented upon guinea-pigs, rats, cats, and dogs, as well as rabbits. I myself operated upon monkeys, the wounds being perforating wounds of the posterior part of the ciliary region from without in, and injuries or perforating wounds of the fundus from within out.

According to Krückmann, the invasion of the wound and neighbouring parts by leucocytes is the prominent feature four to six hours after the operation. These leucocytes are poured forth from all the blood-vessels available, viz. those of the episclera, choroid, and such sclerotic vessels as are to be found. They are carried from all sides into the wound, which they block, the groups being thickest along the edges. They penetrate into the dilated lymphatic channels between the scleral lamellæ ("Infiltrations-scleritis" of Alt). The meshes of the supra-choroidea are also packed with them. Their function is largely a phagocytic one, directed to the removal of the parts injured beyond repair. The edges of the wound become smooth and glazed, so that the process differs in no essential from that which occurs in other parts of the body. In the course of the second day the leucocytes begin to disappear, their duty as scavengers having been accomplished.

Franke describes the new formation of round- and spindle-shaped cells during this period by a process of amitotic division. The need for rapid increase of cells in all acute inflammatory processes results in division by fission, gemmation, etc., ordinary karyokinesis being apparently too slow. This is seen *par excellence* in the cornea. It is not surprising that some increase of the cells present should occur at this early stage, but it is probable that most of them are leucocytes (Krückmann, Stoewer), and that the process described by Franke plays a very subsidiary part.

Franke observed the evidences of karyokinesis after forty-three hours, which agrees well with the time assigned by Krückmann for the commencement of the second stage, viz. the process of repair. By this

time the detritus and perhaps much of the fibrinous coagulum which formed a large part of the inflammatory exudate have been removed by the agency of the leucocytes, and these themselves have in turn largely disappeared. It is now that the activity of the fixed tissue elements forms a leading feature, and as in other parts of the body, the blood-vessels are the most important. In the episcleral tissue and conjunctiva, in the interstices of the neighbouring muscle-fibres, and in the choroid, many cells are seen dividing by mitosis, but especially those belonging to the adventitia of the blood-vessels. These (probably including the plasma-cells) proliferate rapidly, forming spindle-shaped cells, *i. e.* embryonic fibrous tissue, which invade the wound area, accompanied by new-formed capillaries. Many types of cells are seen in many stages of proliferation, but besides those already mentioned endothelial cells are very prominent. The scanty scleral corpuscles are not inactive, but also proliferate. They do not appear, however, to invade the wound area until a later period. The leucocytes play no part in the process of repair. The vitreous has a purely passive part in the process, except that it becomes fibrillated (Franke). The retina is also passive, becoming glued down to the choroid and locally degenerated. The retinal vessels probably play a small part in common with those of the choroid. (*See* 'Wounds of the Retina.')

Düffing examined an eye microscopically four weeks after a double perforating wound of the sclerotic by a small saw. He found that the fibres of the scar now had the same direction as those of the normal sclera, and passed imperceptibly into the surrounding normal tissue. This result was confirmed by Franke's experiments on rabbits. It is at this stage in all probability that the normal sclerotic corpuscles manifest their influence. They probably reproduce themselves slowly, and partially replace the scar tissue. It is not unlikely, too, that they influence the polarity and character of the newly formed fibrous tissue, tending to mould the new cells gradually to their own type. Such an "infective" influence of one cell upon its neighbours is not uncommon in many pathological conditions (*e. g.* new growths), but where the injured normal cells are of a high degree of differentiation the process usually stops short at a lower grade, as is seen in the latest stages of scars in the cornea. These become more allied to sclerotic cells than to corneal corpuscles, possibly a form of atavism. In the case of the sclerotic itself the lowly grade of cell is more readily approximated by the new-formed corpuscles. The tissue, however, though much resembling the normal sclerotic, is never absolutely normal; the fibrils lie much more closely packed and are not so sharply divided into bundles, and, as in scar tissue generally, the typical lymph-spaces are absent.

Krückmann draws a distinction between the more cellular "scar tissue" (*Narbengewebe*) on the inner and outer surfaces and the "compensatory or substitutive tissue" (*Ersatzgewebe*) interposed between the lips of the scleral wound.

I have examined a large number of human eyes with perforating wounds, and have given detailed descriptions of three cases, four, eight, and nineteen days respectively after the receipt of the injury. Besides the length of time there are other factors which have to be taken into

consideration. Experimental lesions are clean cut and aseptic; injuries and ruptures are often ragged, and in nearly all cases which reach the pathological laboratory they either are in a very early stage or are septic. In these there is very often little or no attempt at repair.

LJUBINSKY.—A. f. O., xiii, 2, 1867. ROTH.—Virchow's Archiv, lv. MIYSHITA.—Inaug. Diss., Würzburg, 1888. BAQUIS.—Ziegler's Beiträge, iv. TEPLJASCHIN.—A. f. A., xxviii, 1894. FRANKE.—A. f. O., xli, 3, 1895. KRÜCKMANN.—A f. O., xlii, 4, 1896. STOEWER.—A. f. O., xlvi, 4, 1898. PARSONS.—R. L. O. H. Rep., xv, 3, 1903. DÜFFING.—A. f. O., xl, 2, 1894. MELLER.—A. f. A., xliii, 1, 1901.

INFLAMMATION

Inflammation of the sclerotic is one of the rarer affections of the eye, and is always limited in the ordinary types to the anterior segment between the margin of the cornea and the equator. It is impossible, pathologically, to draw any hard and fast line between the deeper forms of conjunctivitis, or *episcleritis*, and true inflammation of the sclerotic itself, or *scleritis*. In the very limited number of cases which have been examined microscopically the general type of inflammation has been characteristic, but the relative extent has varied considerably and apparently out of all proportion to the clinical severity. There are also differences in detail which make any pathological classification at present uncertain and incomplete. Even clinically episcleritis merges into scleritis, and the latter, though usually nodular like the former, is invariably more diffuse, and in rare cases invades the circumcorneal area. The superficial and deep forms will be described separately, though it is important to remember that no accurate line of demarcation can be drawn between them pathologically any more than clinically.

EPISCLERITIS

In episcleritis a circumscribed nodule, which may be as large as a lentil, is formed. It is hard, immovable, and very sensitive to the touch, the injected conjunctiva moving freely over it. It is traversed by the deeper episcleral vessels, and therefore appears violet in colour. It is extremely chronic, often occurs in other regions of the circumcorneal zone, never ulcerates, and may be entirely absorbed, but more frequently leaves a slate-coloured scar behind, to which the conjunctiva is adherent. The cornea and uveal tract rarely participate in the inflammation.

Microscopically the nodule is seen to be caused by an inflammatory round-celled infiltration, which chiefly involves the deep layers of the episclera, but also invades the superficial laminæ of the sclerotic, which are separated by œdema, the lymphocytes lying in rows or in spindle-shaped masses between them. The conjunctiva is also infiltrated, mostly in the subepithelial layers, the middle layers being least affected (Schirmer). The lymphocytes are also very numerous around the blood-vessels, which are widely dilated and filled with blood. Extrava-

sations of blood are also sometimes present (Uhthoff, Schirmer). The lymphatics are also extremely dilated, especially in the superficial layers. Their endothelial linings are intact, and they contain a fine granular coagulum in their lumina. The œdematous exudates not infrequently coagulate, forming networks of fibrin with entangled leucocytes. The lymphocytes are often very thickly packed, and make up the greater part of the nodule. The fixed connective-tissue cells do not apparently proliferate (Schirmer).

All these changes may completely disappear, though vascular congestion often persists for a long time. On the other hand, some of the superficial scleral lamellæ usually necrose, though to only a very limited extent, a slight thinning of the sclerotic being the result (Wedl and Bock).

Episcleritis periodica fugax, first described as *subconjunctivitis* by v. Graefe, and later by Hutchinson, Nettleship, Fuchs, and others, has not been examined microscopically.

Scleritis

In the deeper forms of scleritis, which are much rarer, there are also nodules, but these are usually less circumscribed. The swelling is at first dark red or bluish, later it becomes pale violet and semi-transparent, like porcelain. It may extend entirely round the cornea. The condition differs from episcleritis in that the cornea and uveal tract are invariably involved, but whether primarily or secondarily is uncertain (*see* "Annular Scleritis"). There is no ulceration, but much absorption, so that the sclerotic is thinned, a dark purple cicatrix being formed, which is often unable to resist the intra-ocular pressure, so that ectasia follows. Young adults generally suffer, and both eyes are commonly affected. In many cases of diffuse deep scleritis hard whitish nodules develop in the inflamed zone. They are the size of a pin's head, and lie beneath the conjunctiva, all at much the same distance from the corneal margin (Fuchs). They disappear without disintegrating.

Microscopically the typical features of episcleritis are often present in addition to the deep scleritis (Kostenitsch). The sclerotic is, however, most infiltrated in the middle layers (Kostenitsch, Schirmer). The cells are chiefly mononuclear lymphocytes, but polymorphonuclear leucocytes and extravasted red corpuscles are also found. Friedland found giant-cells both in the sclerotic nodules and in the choroid, but it is doubtful if this was an ordinary case of scleritis (*v. infra*).

Kostenitsch found the scleral cells and vessels increased; the lamellæ normal, but separated in places by exudate. The infiltrating cells between the lamellæ extended forwards into the cornea, setting up sclerosing keratitis, and backwards into the iris and ciliary body (*see* Fuchs' Text-book, fig. 64). Schirmer also found the blood-vessels increased, especially in the outer layers. They were much dilated and surrounded by lymphocytes. The scleral fibres were swollen and œdematous, staining deeply with hæmatoxylin.

In the more severe cases the laminæ of the sclerotic are pushed apart, as in glaucomatous eyes (Birnbacher and Czermak), and indeed, glaucoma is not infrequently present. In other cases the tension is subnormal (Steffens). Schirmer found this separation of the bundles most in the inner layers, which were also peculiarly plexiform. Some were granular, and the nuclei were diminished in number.

Later many fibres and cells necrose, or undergo fatty or hyaline degeneration. They are then slowly absorbed, without ulceration. Rarely the lymphocytes necrose, their nuclei staining more faintly. The elastic fibres also break up and are gradually absorbed. Accompanying these degenerative changes the vessels undergo sclerosis, the endothelium proliferating.

According to Schirmer, proliferation of new fibrous tissue may replace atrophy. He found an equatorial nodule with a thick mass of young granulation tissue. Baumgarten found great thickening of the sclerotic (4 mm.), due partly to increase in scleral fibres, partly to infiltration with round-cells. The overgrowth in these cases may be diffuse or circumscribed, simulating a tumour (fibroma or sarcoma). The condition has been called *hyperplastic scleritis* (Schöbl).

Vossius, in a case of typical nodular scleritis, observed greyish yellow nodules such as those described by Fuchs. They were accompanied by lymphatic cysts, which were seen clinically. One of the larger nodules was examined microscopically. The subepithelial tissue was densely infiltrated with leucocytes; these faded off internally into the main mass, which was chiefly composed of endothelial (epithelioid) cells with faintly staining nuclei. There was no infiltration below, but the lymphatics were dilated both superficially and deeply. There were no giant-cells or caseation, and inoculation of the anterior chamber of rabbits was negative.

The sclerotic nodules show a predisposition to attack the neighbourhood of the anterior perforating ciliary vessels, and extension of the inflammation is usually along them. In many cases the inflammation is equally marked in the sclerotic and in the uveal tract. In these it is impossible to draw any deductions as to priority of onset. Kostenitsch and Schirmer regard the uveitis as primary. The latter thinks that there is always a combined sclero-episcleritis in those cases in which nodules are seen clinically, whilst cases with violet discolouration of the sclera and little prominence may be due to a pure scleritis. In one of Friedland's cases there was also choroiditis, but the patches did not correspond with those of the scleritis. This may be explained by transmission along the vessels and lymph-channels, but is regarded by this author as evidence of independent foci of inflammation.

Ulceration as a result of ordinary scleritis must be regarded as of extreme rarity, yet such a case has been reported by Holthouse, and examined microscopically by Treacher Collins. It occurred in a woman æt. 71; there was no history of tubercle or syphilis. The early course was that of typical episcleritis, but later ulceration occurred in two places over one nodule. The tension became −1, and the globe later became shrunken, and was excised. There were no giant-cells, nor were tubercle bacilli found.

Allied to scleritis are the cases described by Coppez and Gayet. In these there was invasion from the orbit by tumours of uncertain—possibly lymphadenomatous—nature.

Coppez says: "The corneal limbus has disappeared. There is no definite limit between sclera and cornea, but a rosy white substance occurs astride the two membranes, and is prolonged under the conjunctiva."

Gayet says: "At the limbus of the cornea there was a circle of round infiltrates of white or yellowish-white colour, more or less saturated, nearly touching each other, and forming a ring round a perfectly clear and transparent centre."

SCHIRMER.—A. f. O., xli, 4, 1895. UHTHOFF.—A. f. O., xxix, 3, 1883; xlix, 3, 1900. WEDL AND BOCK.—Path. Anat. des Auges, Wien, 1886. KOSTRNITSCH.—A. f. A., xxviii, 1894. BIRNBACHER AND CZERMAK.—A. f. O., xxxii, 2, 1886. STEFFENS.—K. M. f. A., xli, 1903. BAUMGARTEN.—A. f. O., xxii, 2, 1876. SCHÖBL.—A. f. A., xx, 1889. VOSSIUS.—Ophth. Klinik, iv, 1900. FRIEDLAND.—A. f. O., xlviii, 2, 1899. HOLTHOUSE.—R. L. O. H. Rep., xiii, 1893. COPPEZ.—A. d'O., xv, 1895. GAYET.—A. d'O., vi, 1886; viii, 1888. EPISCLERITIS PERIODICA FUGAX:—HUTCHINSON.—T. O. S., v, 1885. NETTLESHIP.—T. O. S., viii, 1888. FUCHS.—A. f. O., xli, 4. 1895.

ANNULAR SCLERITIS

A group of severe cases of scleritis has been isolated by German authors under the term *brawny infiltration of the sclerotic* (*Sulzige Infiltration der Sclera*). As this nomenclature is not very satisfactory I have suggested the term *annular scleritis*.

Unlike ordinary scleritis, which usually attacks young adults affected with tubercle or congenital syphilis, annular scleritis is a disease of advanced age. All the cases recorded have been in patients over sixty years of age, and most of them were women. Both eyes are usually affected, though often to a very unequal extent. The progress of the disease is extremely chronic, with periodic exacerbations and remissions. The prognosis is very bad, most of the eyes being lost; hence the large number which have been examined microscopically as compared with ordinary scleritis, pathological reports of which are extremely rare.

The locality and extent of the infiltration is characteristic. Even when typical scleritis invades the whole circumcorneal area it leaves the limbus itself free, thus differing from phlyctenular nodules. Here, on the other hand, the corneal margin is the essential site of the affection, and from this spot the infiltration spreads on both sides into the neighbouring tissues, having a sharp edge on the side of the cornea, which it partly overlaps, and gradually passing into normal tissue on the side of the sclerotic. In advanced cases extension continues in each direction, so that it reaches the equator posteriorly, but never much exceeds this level, whilst anteriorly it invades the cornea as a peripheral sclerosing keratitis, ever advancing slowly towards the centre.

The appearances of the infiltration were sufficiently characteristic to lead Schlodtmann to identify the complaint by them. In other cases the existence of the scleritis has only been discovered subsequently to the removal of the eye. In typical cases the swelling is gelatinous and succulent, and has a brownish-red colour.

Besides the cornea, the uveal tract is usually inflamed, especially the anterior part of the choroid and the ciliary body. As in the case of ordinary scleritis, discussion has arisen as to whether this uveitis is secondary to the scleritis or causal. In each case it is probably a secondary phenomenon, sometimes a true sequel, at others a mere concomitant.

There are three records of microscopical examination of annular scleritis. Schlodtmann describes three cases clinically, one of them

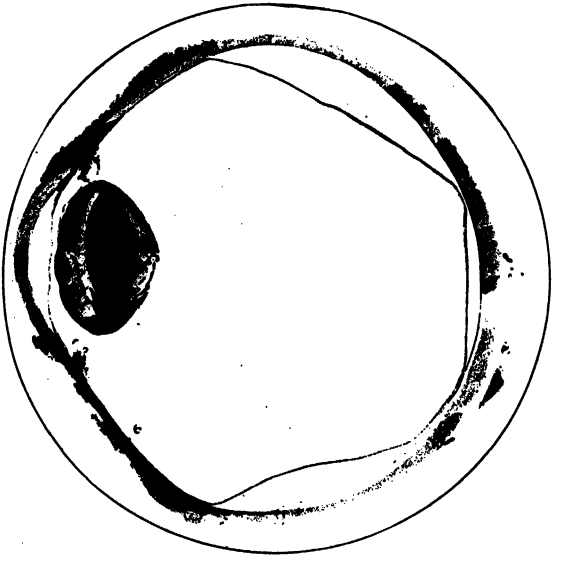


FIG. 182.—ANNULAR SCLERITIS. × 3.
Holmes Spicer and Parsons, T. O. S., xxii.

pathologically. The patient was aged seventy-four. The conjunctiva was reddened for about 5 mm. around the cornea, traversed by large vessels, and raised by a brawny, reddish-brown thickening above the underlying tissue. In this area there was enormous dilatation of blood-vessels and lymphatics, the latter forming cavernous spaces under the epithelium. In the deeper layers was an intense leucocytic infiltration, containing numerous necrotic masses, communicating with each other in a plexiform manner. Giant-cells were present to an enormous number. No tubercle bacilli could be found.

In Friedland's case the distribution was the same; there was no tendency to suppuration, and Friedland points out that the leucocytes were all mononuclear cells with a relatively large necleus and little

protoplasm. Distinct degenerative processes (breaking up of nuclei, amorphous material, etc.) were present both in the scleral fibres and also amongst the round-cells. The absence of giant-cells, epithelioid cells and bacilli was considered sufficient to exclude tubercle. There was no evidence, clinical or pathological, of syphilis, gout, or rheumatism. In one eye choroiditis came on late and led to failure of sight; in the other no uveitis occurred. Friedland regards the scleritis and choroiditis as "primary independent diseases arising from a common cause."

Uhthoff's case was similar in localisation, extent, and general histological conditions. There were no giant-cells, the round-cells were all mononuclear, showing marked nuclear degeneration, and the

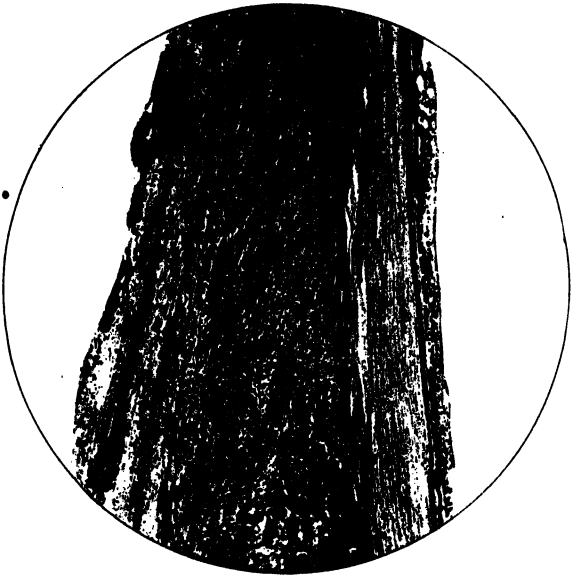


FIG. 183.—ANNULAR SCLERITIS. × 55.

From just behind the ora serrata. Note the dense infiltration of the sclerotic, the laminæ of which are separated by round-cells. The choroid and retina are much degenerated.

lymphatics and blood-vessels were dilated. The author draws attention to the thickening of the walls of the blood-vessels, with endothelial proliferation, leading to partial and even complete blocking of the lumina; and regards the obstruction to circulation as an important factor in the disease. There were distinct nodules in places, recalling trachoma follicles, composed of a central mass of endothelial cells surrounded by a zone of infiltration. No micro-organisms could be found.

The case which I have examined was a woman, æt. 68, whose left eye had been injured two years previously by a blow. Both eyes were

inflamed; the vision of the right was $\frac{6}{6}$. The left had annular scleritis, keratitis punctata, iritis, opacities in the lens, arterio-sclerosis, cystic retina at posterior pole, and increased tension with cupped disc (Fig. 182). The scleritis was found to extend entirely round the anterior part of the globe, and back to the equator. It is deepest above, where the sclerotic is reduced to extreme thinness, only about half a dozen lamellæ remaining intact. The superficial lamellæ are separated from each other and partly destroyed by dense infiltration with mononuclear lymphocytes (Fig. 183). The blood-vessels have proliferated, and are dilated and full of blood-corpuscles. Some polymorphonuclear leucocytes are found near the blood-vessels, especially in the episcleral tissue. In places there are signs of endothelial proliferation in the vessels, but this is not marked. The infiltration is diffuse, and there are no nodules, nor are there any giant-cells.

In this case the inflammatory and degenerative changes are so widespread that it is impossible to be sure of their relative sequence. Uveitis is considered to be the precursor of ordinary scleritis by Arlt, Kostenitsch, Schirmer, Greeff, and others. The direction of the lymph-stream, and the facility of transmission along the course of the anterior ciliary vessels are in favour of this view. The essential identity of the processes in episcleritis and scleritis, the invariable absence of uveitis in pure episcleritis and its almost constant presence in severe cases of scleritis, however, point to uveitis as a sequel rather than as a causal agent. Moreover, it is probable that scleritis often occurs without being diagnosed, and in the absence of any evidence of uveitis. Friedland, too, in a case of typical scleritis, found that the patches of choroiditis did not correspond in position with the nodules of scleritis.

The extreme chronicity of all forms of the disease points to a specific inflammatory process, a view which is borne out by the nature of the leucocytes present. The advance is doubtless impeded by the extreme resistance of scleral tissue to invasions of all kinds, inflammatory or neoplastic; and perhaps also by its direction contrary to the normal lymph-flow.

The line of exit of the venæ vorticosæ seems to limit the backward progress of the inflammation; and this is possibly due to better nutrition of the sclerotic behind the equator.

Schlodtmann's case, although the one which was first described of this kind of scleritis, is open to another interpretation. It may well be a severe case of the granulomatous type of infiltration. To this class probably belong the cases recorded by Brailey, Donald Gunn, and others (*v.* p. 278).

The presence of large numbers of giant-cells in Schlodtmann's case points to its being of different origin to the other cases. In the absence of definite tubercles with caseation, and considering the inability to find tubercle bacilli, the giant-cells may have been ordinary foreign-body giant-cells (Fremdkörper-Riesenzellen) such as are found in granulation tissue. However this may be, there can be little doubt that the severer cases of deep scleritis show definite characteristics as regards localisation, nature of infiltration, etc., which justify their being classed apart.

* PARSONS.—Ophth. Rev., 1902: *see also* SPICER, T. O. S., xxii, 1902. SCHLODTMANN.—A. f. O., xliii, 1, 1897. FRIEDLAND.—A. f. O., xlviii, 2, 1899. UHTHOFF.—A. f. O., xlix, 3, 1900.

PURULENT SCLERITIS

Ulceration and suppuration of the sclerotic are of extreme rarity. The sclera possesses great resistance against invasion both by acute inflammatory processes and by new growths. In purulent panophthalmitis the inner surface of the sclera is usually smooth and unaffected; it is only in very late stages that it becomes eroded, and may be perforated. In these cases the perforation is generally in front of the equator; the inflammation travels along the course of the anterior ciliary vessels, and perforation takes place at the corneo-scleral margin. Arlt pointed out that it is the sclera and not the cornea which is thus perforated. He also first described a case of purulent scleritis.

In Schlodtmann's first case the intense leucocytic infiltration with marked necrosis is suggestive of actual suppuration, but there is no definite information as to the nature of the leucocytes nor of definite suppuration.

It is doubtful whether abscess, in the ordinary sense of the word, ever occurs in the sclera. Suppuration is almost invariably the result of purulent choroiditis, resulting from an intra-ocular foreign body, and panophthalmitis from other causes. Groups of leucocytes are often found in the later stages in the inner layers of the sclera, and these may burst into the vitreous, producing ulcerated patches. They lead to over-production of fibrous tissue, which pierces the choroid and retina, and forms a knob-like mass in the vitreous. In severer cases the globe is ruptured, and Alt regards the equator as the usual site, at the exit of the venæ vorticosæ. The consensus of opinion is, however, in favour of the weak spot of the eye, viz. the corneo-scleral margin, and the cases in which the rupture takes place at the equator are exceptional, and are probably due to previous blocking of the angle of the anterior chamber, which becomes stronger by the deposition of new fibrous tissue.

As in a case described by Alt, the process may be extremely rapid, so that the swollen sclera resembles a staphyloma. In this case the sclera was six times its normal thickness, and, together with the episcleral tissue, was intensely infiltrated with leucocytes.

Alt regards implication of the ciliary nerves as a factor in the production of sympathetic ophthalmia.

Ulceration from outside is even rarer than from within. von Graefe describes a case after a strabismus operation; and suppurating sutures, with ulceration of the neighbouring sclera, must have been seen by many surgeons, though they have not been recorded.

Abscesses on the surface of the sclerotic have been described by Boyd in glanders.

ARLT.—Die Krankheiten des Auges, ii, p. 11. ALT.—Lectures on the Human Eye, p. 44, New York, 1880. v. GRAEFE.—A. f. O., iii, 2, 1857. BOYD.—Tr. Path. Soc., xxxiii.

Syphilis

Gummata of the ciliary body, etc., may often lead to destruction of the sclerotic. They then appear clinically as gummata of the sclerotic, and have often been described as such. In many of the cases, indeed, it is impossible to be certain where the disease actually commenced, and when we remember the frequency of gummatous deposits in the connective tissues, it would be strange if they did not occasionally occur in the sclerotic.

Alexander found eight cases of gumma, limited to the sclerotic, in the literature. An earlier case recorded by Bull is not included. In Hirschberg's case, a girl of fifteen, there was a swelling from the limbus to the equator. Rothmund and Eversbusch recorded two cases, and two were also recorded by Higgens. In one of the latter there were three nodules. Others have been described by Andrews, Minor, Alt, and others, and Donald Gunn's cases probably belong to the same category.

The disease has never been examined microscopically, except in cases in which there has been extensive affection of other parts. The histological characters are then similar to those found in the cases of gumma of the ciliary body which I have described (*v. infra*).

Gummatous disease of the episclera occurs, and may be difficult to differentiate from other conditions of the episclera and conjunctiva. An interesting case, in which there were giant-cells, has been described by Peppmüller, but tubercle bacilli were finally found after prolonged search. I have seen an exactly similar case, and in both the disease rapidly cleared up under antisyphilitic treatment (*v.* p. 78).

Alexander.—Syphilis und Auge, Wiesbaden, 1889. Bull.—Tr. Amer. O. S., 1874. Hirschberg.—In Nagel's Jahresb., 1877. Rothmund and Eversbusch.—Mittheilungen aus der k. Universitätsklinik zu München, 1882. Higgens.—Brit. Med. Jl., 1882. Andrews.—A. of O., xi, 1882. Minor.—A. of O., xiv, 1885. Alt.—Amer. Jl. of Ophth., 1893. Donald Gunn.—T. O. S., xiv, 1894. Peppmüller.—A. f. O., xlix and l, 1900.

Tubercle

It is doubtful whether primary tubercle of the sclerotic exists. It is frequently invaded secondarily to the uveal tract.

Köhler reports a case in which the choroid and Tenon's capsule were but slightly affected with miliary tubercles, whilst the sclerotic was the seat of a caseous mass, projecting 4 mm., at a spot 3 mm. outside the optic nerve. Around the necrotic, diffusely staining material were giant-cell systems with epithelioid cells. There were miliary tubercles in the sclerotic in the neighbourhood.

Brailey's case of scleritis was probably tubercular; it occurred in the left eye of a scrofulous child of nine and a half with enlarged cervical glands. The episcleral tissue was thickened and greyish in colour, the surface breaking down and ulcerating in several places after a few weeks' duration of the disease. Portions removed for diagnosis showed tubercular nodules with lymphoid infiltration, giant-cells, and definite caseation. Tubercle bacilli could not be demonstrated.

Müller also described a cyst in the sclerotic, the walls of which were composed of miliary tubercles.

Schlodtmann's case (*v.* p. 276) may perhaps also have been tubercular or syphilitic, and a case of cyclo-scleritis described by Utermöhlen was almost certainly tubercular.

The sclerotic is often much thickened by fibrous deposits over uveal tubercles (Liebrecht). Perforation, with the formation of a tubercular ulcer, occurs most commonly at the site of the anterior perforating ciliary vessels.

Köhler.—Dissertation, Würzburg, 1884. Brailey.—T. O. S., ix, 1889. Müller.—Wiener med. Presse, 1890. Utermöhlen.—Diss., Amsterdam, 1902; *see* Steffens, K. M. f. A., xli, 1903. Liebrecht.—A. f. O., xxxvi, 4, 1890.

Leprosy

Episcleral nodules occur in leprosy, and have the usual characteristics (*v.* p. 7). In the sclerotic the conditions of extension are impeded by the denseness of the tissue, but slow invasion takes place along the perivascular and interlamellar lymph-spaces. The lamellæ, including the elastic fibres, are destroyed. The lepra bacilli often form spindle-shaped masses and long rows, around which there are only few round-cells. This arrangement resembles that found in the cornea, but is less regular. Lie was unable to find bacilli in the posterior part of the sclerotic.

(For Bibliography, *see* "Lids," "Cornea.")

Degenerations

Hyaline degeneration of the scleral laminæ is found under pinguecula, and in other degenerative conditions.

Fatty degeneration occurs in old age, and in inflammatory conditions.

Calcification also occurs sometimes after old inflammatory processes, and in old age. After removal of the lime-salts the scleral lamellæ show an apparently normal histological structure. In rare cases actual bone formation may take place.

Cysts

Several cases of cyst of the sclerotic have been reported, but few have been examined microscopically. Some cystic cicatrices, implantation cysts, etc., might easily be mistaken for them. Mackenzie and Hasner recorded cases clinically.

Colbourn described a corneo-scleral cyst containing clear fluid in a boy æt. 15; both the inner and outer walls consisted of corneo-scleral

tissues. The author could find only two similar cases in the literature. one due to a fragment of steel, the other to a cysticercus.

Rogman saw a cyst near the cornea in a child of thirteen. It was trilobate, and contained clear fluid. Microscopic examination of the outer wall showed that it consisted of fibrous tissue covered with conjunctival epithelium. There was no epithelium or endothelium on the inner surface.

Lagrange described a scleral cyst following a strabismus operation. There was no histological examination.

Congenital cysts are not truly cysts of the sclerotic, but are due to defects of development in that and the other membranes.

MACKENZIE.—Diseases of the Eye, ii, London, 1854. HASNER.—Klin. Vorträge über Augenheilkunde, Prag, 1860. COLBURN.—Jl. of the Amer. Ass., 1896. ROGMAN.—Ann. d'Oc., cxvii, 1897. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901.

TUMOURS

BENIGN TUMOURS

Hyperplasia, though not actually a tumour formation, may be conveniently mentioned here. The sclerotic often looks enormously thickened in shrunken globes. Thickening is here more apparent than real, and is due to contraction of the elastic tissues and folding; there is, however, often evidence of inflammatory hyperplasia. Wounds and localised inflammatory processes usually lead to thinning, owing to the action of the normal or increased intra-ocular tension. They occasionally cause localised thickening. The histological process and results are identical with the healing of scleral wounds (*v.* p. 267), except that the development of cicatricial tissue is excessive.

Enormous deposits of scar tissue may be found around foreign bodies embedded in the sclerotic.

Thickening may be due to enormous infiltration with round-cells (Schöbl). Gayet described the simultaneous occurrence of this condition in both eyes, and attributed it to a bacterial origin.

Fibroma of the sclerotic has been described in a unique case by Saemisch. It was situated near the posterior part on the inner side; there were many signs of inflammation in other parts of the eye. Most probably the case was one of inflammatory hyperplasia.

Fibro-chondroma near the limbus in a child of nine months has been reported by Castaldo. It was probably a teratoid epibulbar growth. Cartilage has often been found in the sclerotic in congenital malformations. It may be a reversion to the avian type.

Osteoma, described by Blasius, and by Watson, have probably the same explanation, though in the latter case it was situated between the superior and internal recti, a rather unusual situation for congenital growths. Moreover, the occurrence of bone in the sclerotic of lower animals normally, and its rare occurrence in man following inflammatory and senile changes must be borne in mind.

Telangiectasis in the sclerotic has been described by Quaglino. The growths were multiple and were probably episcleral.

SCHÖBL.—A. f. A., xx, 1889. GAVET.—A. d'O., viii, 1888. SAEMISCH.—A. f. A., ii, 1872. CASTALDO.—Riv. di Ott., 1893. BLASIUS.—In MACKENZIE, Diseases of the Eye, ii, 1854. WATSON.—Tr. Path. Soc., xxii. QUAGLINO.—Ann. di Ott., ii, 1872.

MALIGNANT TUMOURS

Eliminating conjunctival and episcleral sarcoma, there is no indubitable case of **primary sarcoma** of the sclerotic. As Lagrange points out, the question is allied to the very doubtful occurrence of sarcoma in tendons. The earlier cases described by Hirschberg, Neumann, Gorecki, etc., are open to doubt, and would probably be classified otherwise now. The most likely case is a melanotic sarcoma reported by Achenbach. It occurred around a posterior ciliary nerve, the optic nerve and choroid being normal. The author considered that it arose from the pigmented perineural tissue.

Secondary sarcoma of the sclerotic is of course common when that disease attacks the uveal tract. It arises almost exclusively by propagation along the perivascular and perineural lymph-spaces, though malignant thrombi may occur in the vessels.

Secondary carcinoma of the sclerotic arises from metastatic carcinoma of the choroid in exactly the same manner.

Secondary epithelioma of the sclerotic arises by continuity from epithelioma of the limbus.

Secondary glioma of the sclerotic arises from glioma of the retina by continuity with secondary extensions in the choroid along the perforating vessels, and also by invasion of the interlamellar spaces. The lamellæ are very resistant, and remnants persist almost indefinitely.

HIRSCHBERG.—K. M. f. A., vi, 1868. ACHENBACH.—Virchow's Archiv, cxliii, 1896.

CHAPTER V

THE IRIS AND ANTERIOR CHAMBER

THE NORMAL IRIS AND ANTERIOR CHAMBER

THE ciliary body may be considered roughly to be shaped like an isosceles triangle with the apex directed backwards (Fig. 184). The iris does not spring from the outer angle of the base, but from near the middle; consequently part of the anterior surface of the ciliary body enters into the formation of the anterior chamber.

In lower mammals and in the human fœtus the angle of the anterior chamber is occupied by a meshwork of fibres, stretching from the back of the anterior part of the sclerotic to the ciliary body and the root of the iris. Indeed, it pushes its way backwards for a short distance between the ciliary muscle and the ciliary processes. Looked at from within, this network resembles the teeth of a comb, and was hence called the *ligamentum pectinatum iridis* (Hueck). The maze of meshes between the trabeculæ were investigated by Fontana, and are called the *spaces of Fontana*. The fully developed ligamentum pectinatum consists of two parts: an outer more compact part, lying in apposition with the sclerotic, and forming the inner wall of the great venous plexus, the *canal of Schlemm;* and an inner looser part. The latter persists in man until the sixth fœtal month (Rochon-Duvigneaud, Treacher Collins), after which it disappears, and with it disappear most of the spaces of Fontana, which can scarcely be said to exist in the adult. The fœtal condition is often retained in microphthalmic eyes (Fig. 185). Rochon-Duvigneaud called the outer persistent portion the sclero-corneal trabecular system, and looked upon it as derived by dissociation from the inner circular lamellæ of the sclerotic.

The ligamentum pectinatum iridis consists of trabeculæ of fibrous tissue, made up of bundles of fine fibrillæ. The finer details of the arrangement of the trabeculæ have recently been investigated by Asayama. Descemet's membrane splits up at the periphery into fibres, which pass into the trabeculæ; but these do not take on Weigert's elastic-tissue stain deeply. The trabeculæ are covered by endothelial cells with large oval or round nuclei; these are continuous with those of Descemet's membrane and with those covering the iris.

The canal of Schlemm is really a venous plexus surrounding the

angle of the chamber, and lying in the inner part of the extreme anterior part of the sclerotic. In meridional section it is usually oval, but is often irregular, or cut twice in the same section, showing that it is convoluted and also plexiform. It is lined by endothelium lying on a fine fibrous basis, which separates it from the endothelium of the spaces of Fontana. There is therefore a thin membrane between the canal of Schlemm and the anterior chamber, a fact which has also been demonstrated by filtration experiments. The trabeculæ often have pigment-cells, especially in old people, usually most in the posterior part.

The iris is made up principally of vessels, nerves, and unstriped muscle, bound together by a very loose cellular stroma. This consists of a small amount of fine fibrous tissue, with branching spindle- and star-shaped cells, with long interlocking processes: most of them contain brown pigment granules, varying in amount according to the

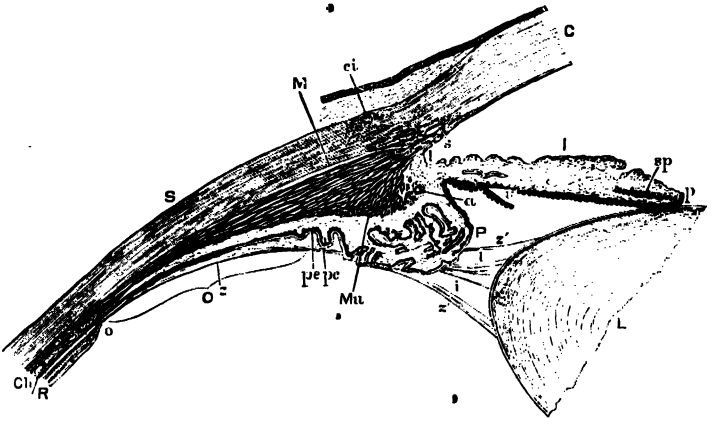


FIG. 184.—THE NORMAL CILIARY REGION.

From Lawson, after Fuchs. S, sclerotic; C, cornea; L, lens; R, retina; Ch, choroid; I, iris; P, ciliary processes; M, longitudinal fibres of ciliary muscle; Mu, circular fibres of ciliary muscle; l, ligamentum pectinatum; s, canal of Schlemm; a, circulus iridis major; sp, sphincter pupillæ; v, retinal pigment epithelium, turning forwards at pupil, p; ci, anterior ciliary vessels; O, pars plana of ciliary body; o, ora serrata; z z', zonulæ of Zinn; i, canal of Petit; pe, pc, layers of pars ciliaris retinæ.

colour of the iris, and absent in albinos. The vessels run radially with the exception of the circulus arteriosus iridis minor, which is situated a short distance from the pupillary edge. The major arterial circle lies in the ciliary body, at the root of the iris, in man. The vessels have a thin muscular coat and a very thick adventitia.

The posterior part of the stroma near the pupillary edge is occupied by a ring of unstriped muscle, the *sphincter iridis*. This is inserted by oblique off-shoots into the posterior wall, so that the posterior pigment layer is often seen to be drawn into a fold (Grunert).

The anterior surface is irregular, and is covered by endothelium, continuous with that of the ligamentum pectinatum. There are breaks in the continuity of the endothelium leading down into irregular spaces

or *crypts* in the stroma, which thus communicates directly with the anterior chamber. The largest are situated over the circulus minor. They are not lined with endothelium, but fibres covered with endothelium often span the mouths. Fuchs, who has paid particular attention to them, only found them once quite covered in by a fine membrane.

The stroma is denser immediately below the anterior endothelium (*anterior limiting layer*), and very cellular, with little or no fibrous tissue. The cells here are often deeply pigmented, and Baas found groups of round pigment-cells between the endothelium and the stroma. Congenital pigmented spots ("nævi") are not uncommon here (*v. infra.*).

The *posterior limiting layer* of the stroma consists of a fine fibrillary



FIG. 185.—FŒTAL CONDITION OF THE ANGLE. × 18.

Parsons, T. O. S., xxii. From a case of microphthalmos. The angle is filled with spongy tissue, containing well-marked spaces of Fontana; this extends well in front of Schlemm's canal. Other features showing arrest of development are seen in the persistence of the posterior vascular sheath of the lens and the condition of the pars ciliaris retinæ.

membrane (*Bruch's membrane*), probably representing the lamina vitrea of the choroid, but much less conspicuous. In many animals, *e.g.* the albino rabbit, radial unstriped muscle-fibres, are found in and upon this membrane (*dilatator iridis*). These are difficult to demonstrate in man, but must be admitted both on anatomical and physiological grounds.

Juler demonstrated fusiform cells, with rod-shaped nuclei, indistinguishable from unstriped muscle-fibres, in a continuous layer anterior to the pigment epithelium, which had been bleached with euchlorine. Grunert, in bleached flat preparations, found rod-shaped nuclei here, which stained yellow, like the sphincter fibres, with

van Gieson. In the contracted pupil they lay in the limiting layer; in the dilated pupil they projected backwards. It is not certain that these cells were not the spindle-shaped retinal epithelial layer, and indeed, Grunert admits his nuclei into this layer. It would seem *à priori* improbable that epiblastic cells should develop into muscle-fibres, but the phenomenon would not be unique, since the arectores pilorum of the skin are of epiblastic origin. A very elaborate investigation of the subject has been carried out by Szili, Jr., working under van Lenhossék. He concludes that both the sphincter and the dilatator are developed from the retinal epiblast. The former arises at the commencement of the fourth month from the epithelial cells at the junction of the two layers of the secondary optic vesicle. The latter is formed by the transformation of the anterior layer of epithelium in the seventh month. Bruch's membrane forms a continuous layer of fine fibres, and is of unequal thickness up to 7—8 μ; it has no nuclei. It stains yellow with van Gieson, like muscle-tissue. Between it and the posterior epithelium is the dilatator, consisting of low, flat cells, with horizontal oval nuclei. In places between these and the posterior epithelium there are groups of cells with round nuclei; these are epithelial cells of the anterior layer which have not been transformed into muscle.

The dilatator iridis can be easily demonstrated by bleaching with permanganate of potassium and oxalic acid. It stains well by Mallory's neuroglia stain (Verhoeff, Parsons).

The posterior surface of the iris is covered by a double layer of *retinal epithelium* (pars retinalis iridis, pars iridica retinæ). This is deeply pigmented except in albinos, and the shape of the cells can only be made out in bleached sections. The pigment granules are dark brown, mostly round, but some are rod-shaped, like the retinal pigment in lower mammals. The cells are cubical or polygonal, and large in the posterior and superficial layer, and flat and spindle-shaped in the anterior layer. The posterior surface often appears crenated, in which case the cells look wedge shaped, with their apices pointing forwards. At the pupillary edge the layers fuse, and this represents the mouth of the secondary optic vesicle.

Fuchs divides the iris into two parts, the pupillary zone, central to the circulus minor, and the ciliary zone, peripheral to it; the latter being further subdivided from within out into (1) a smooth part, (2) a folded part, with 1—7 concentric contraction (or rather, dilatation) furrows, and (3) a very narrow marginal zone, seen only in blue eyes, especially in children, as a black circle close to the root. This zone has numbers of very small crypts. These zones, and the microscopic structure of the iris, vary with the conditions of contraction or dilatation; and important changes in the relation of the root of the iris to the angle of the anterior chamber also occur.

The meshes of the ligamentum pectinatum are normally elongated in a meridional direction. Heine has shown in monkeys' eyes that in atropin mydriasis the meshes collapse, whilst in eserin miosis they are opened out.

In miosis the pupillary zone is stretched and increased, the crypts

are pulled out into radial slits, and the furrows are flattened out. The retinal layer is pulled farther forwards, so that there is a physiological ectropion of the pigment layer (Grunert). The iris is thinned, the section of the sphincter is elongated and brought parallel to the pigment layer, its pupillary third being slightly bowed forwards (Fuchs). The retinal epithelium is flattened.

In mydriasis the pupillary zone is narrowed and folded in, so that it forms a cup; the pigmented border becomes thin and may disappear. The ciliary zone is narrowed and thrown into concentric folds, the summits of which approach nearer to the back of the cornea, and may nearly touch it. The microscopical appearances are difficult to obtain, since artificial mydriasis soon passes off after removal of the eye. If enucleated during atropin mydriasis and plunged into warm Fleming's solution (Heine), the iris is seen to be thickened, so as to be club-shaped, and the pigment epithelium is crowded together so that the cells are elongated and ride over one another.

ROCHON-DUVIGNEAUD.—Récherches anat. et clin. sur le Glaucome, Paris, 1898. TREACHER COLLINS.—Trans. IX Internat. Congress, Utrecht, 1899. PARSONS.—T. O. S., xxii, 1902. ASAYAMA.—A. f. O., liii, 1, 1901. v. MICHEL.—A. f. O., xxvii, 2, 1881. *FUCHS. —A. f. O., xxxi, 3, 1885. JULER.—Trans. Internat. Congress, Edinburgh, 1894. GRUNERT. —A. f. A., xxxvi, 1898. STOCK.—K. M. f. A., xl, 1902. BAAS.—A. f. O., xlv, 3, 1898. HEINE.—A. f. O., xlix, 1, 1900. *SZILI, JR.—A. f. O., liii, 3, 1902. GUTMANN.—Z. f. A., x, 1903. VERHOEFF.—R. I. O. H. Rep., xv, 4, 1903. *PARSONS.—R. I. O. H. Rep., xvi, 1, 1904.

WOUNDS

In a wound of the iris the tissue retracts and the wound gapes, the aperture being usually filled with blood-clot, which later forms a granular mass in which fibres may be seen. There is little or no formation of granulation tissue unless the iris is prolapsed and exposed; consequently also there is no formation of true scar tissue.

In iridectomy the iris is usually already degenerated, and this may account for the lack of cicatricial reaction. The edges are generally a little thickened, and are later pulled backwards by the contraction of the posterior layers.

Treacher Collins has described a recent iridectomy in which there was a large hæmorrhage into the substance of the iris, and Descemet's membrane was stripped up from the cornea by blood.

Uncomplicated wounds of the iris have received scant attention, and it is probable that important facts might be discovered by re-investigation.

TREACHER COLLINS.—R. I. O. H. Rep., xiii, 1890.

INFLAMMATION

ACUTE IRITIS

Acute iritis has been studied experimentally by v. Michel, and the results are confirmed by the condition found in the iris in human eyes

removed on account of perforating wounds and ulcers, etc. Iritis is best studied in albino rabbits, in which the anterior chamber is first emptied of aqueous and then injected with ¼—½ per cent. silver nitrate solution. The iritis is present after six hours, and v. Michel examined the eyes after six, eight, twelve, and twenty-four hours. He found extensive upheaval of the endothelial layer by fibrinous coagulum, which varied much in breadth. The fibrin formed a fine network, in the meshes of which were leucocytes; these often ran together into clumps. In places the endothelium was destroyed, and the fibrinous coagulum extended into the anterior chamber and into the pupillary area, as well as deep down into the iris stroma itself. It also passed on to the posterior surface of the iris and into the posterior chamber.



FIG. 180.—PLASTIC IRITIS. × 120.

The iris is covered by a delicate network of fibrin, which also passed across the pupil; it is rather indistinct in the figure. The blood-vessels of the iris are dilated and packed with red corpuscles; the stroma is much infiltrated, especially in the anterior layers.

Similar appearances are found in the human eye. The blood-vessels are dilated, packed with red corpuscles and leucocytes, the latter being more numerous than in the normal state. It has not been proved that new vessels are formed, though it is probable. Those frequently described as such clinically occur chiefly in new fibrous tissue, though some are probably merely very dilated normal vessels.

There may be hæmorrhages, but these are commonest in septic iritis. The iris stroma is distended with exudate and infiltrating cells (Fig. 186). The latter consist of lymphocytes, polymorphonuclear leucocytes, and mast-cells; the last named are often present in large numbers. The exudate may be free from fibrin, but this often forms a

well-marked network. In any case it pervades the stroma, often also separating the retinal pigment layers, and extends generally into the anterior chamber and pupillary area. Whether that found in the posterior chamber is derived from the iris or from the ciliary body is uncertain, but the latter source is the more probable, the ciliary body almost invariably partaking more or less in the inflammatory process, at any rate in eyes which are subjected to microscopical examination. Fibrinous coagula do not always raise the endothelium, as stated by v. Michel. They often cover it, and descend into the crypts (Fig. 186). The endothelium often proliferates, especially near the pupillary border, and this doubtless aids the formation of synechiæ.

The pigment epithelium is often broken up in various ways, so that



FIG. 187.—BOMBÉ IRIS. × 10.5.

Very extensive peripheral anterior synechia; posterior synechia with seclusio pupillæ; inflammatory pupillary membrane with occlusio pupillæ; anterior capsular cataract.

cystic spaces are formed between the two layers; these may be empty or filled with fibrin and cells, *débris*, etc. They occur chiefly near the pupil or near the ciliary body. Some of the cells often swell and are cast off, either into the iris stroma or from the free surface. Many lose much of their pigment, free granules being found between the cells, in leucocytes, in the anterior chamber, etc. Clumps of pigment are seen in cells in the iris stroma; these are possibly displaced epithelial cells, but probably most are contained in leucoytes.

Best has demonstrated the presence of globules of glycogen in the exudates in the tissue in iritis.

The fibrinous exudate soon ties down the pupillary edge of the iris to the anterior capsule of the lens, and organisation seems to begin

here very early, resulting in the formation of permanent posterior synechiæ (Fig. 188). Even when the iris becomes subsequently free, the posterior layer of pigment often remains stuck to the lens; the anterior layer is much more intimately attached to the stroma and is torn from

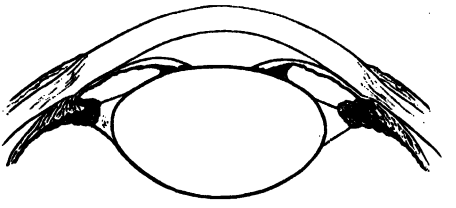


FIG. 188.—SECLUSIO PUPILLÆ.
From Lawson, after Priestley Smith.

the lens. There may be an active proliferation of the retinal epithelium, but this is rarely a marked feature.

Usually, when the synechia gives way, the posterior layer of pigment remains upon the lens capsule, and is torn away entirely from the iris; it gradually atrophies, but remnants often remain permanently. In other cases it is not wholly separated from the iris, but the two layers of pigment epithelium are torn apart, and cystic spaces are produced (*v. infra.*).

If the whole circle of the pupil is tied down to the lens, an *annular or ring synechia* is produced, and the anterior chamber is shut off from the posterior (*seclusio pupillæ*). This condition is full of danger for the eye, leading later to *iris bombé* (Fig. 187), the accumulation of fluid behind the iris causing it to become bulged forward like a sail, so that it looks crateriform from in front. In this manner the periphery is pressed against the cornea and may become adherent; in any case secondary glaucoma results unless the condition is relieved. Sometimes the exudate in the posterior chamber organises entirely. The back of

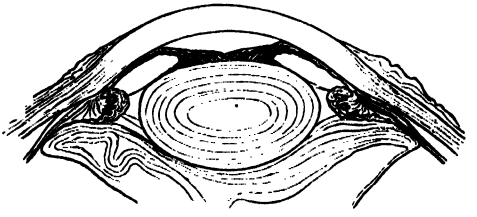


FIG. 189.—OCCLUSIO PUPILLÆ.
From Lawson, after Priestly Smith.

the iris is then tied down to the lens over its whole area, and a *total posterior synechia* results (Fig. 190). The exudate in the pupillary area, again, may organise, an inflammatory pupillary membrane being formed; in this manner the pupil is closed (*occlusio pupillæ*) (Fig. 189).

In mild cases of iritis the exudate is entirely absorbed, and little or no anatomical evidence of previous inflammation may remain. When

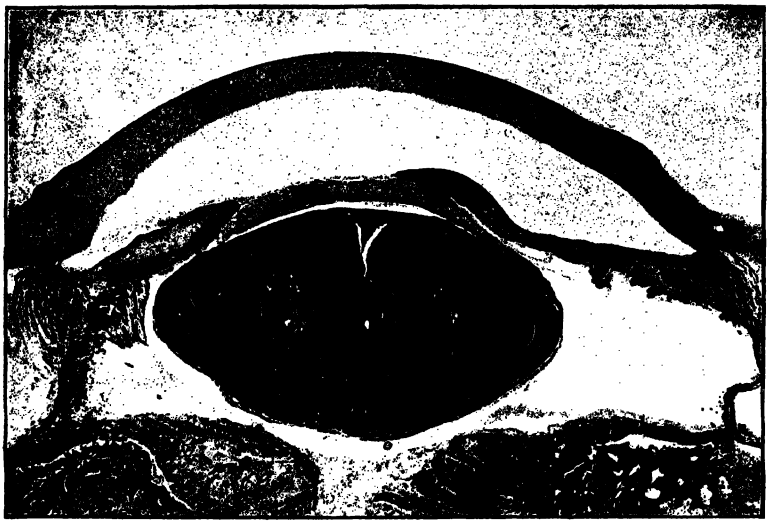


FIG. 190.—TOTAL POSTERIOR SYNECHIA. × 7.

Irido-cyclitis, commencing phthisis bulbi. Total posterior synechia, retraction of periphery of iris; occlusio pupillæ by delicate pupillary membrane. Anterior capsular cataract, calcareous down and to the left. Degeneration of ciliary body and detachment of posterior part. Complete detachment of retina.



FIG. 191.—FIBROUS TISSUE ON IRIS. × 55.

From a microcephalic idiot, æt. 6; irido-cyclitis with detached retina. C, posterior lamellæ of cornea; note k. p. with pigment-cells on left, hyaline nodule with pigment-cells on right; I, iris, inflamed and degenerated, showing fibrinous networks in places; F, laminated fibrous tissue, as thick as the cornea, nearly filling the anterior chamber.

organisation takes place, as in more chronic cases, and where more fibrinous exudates are poured out, the fibrin is transformed into young vascular connective tissue, which forms a layer upon the surface of the iris. The tissue is at first rich in cells, doubtless derived from the fixed connective-tissue cells, and these, with proliferated capillaries, invade the exudates which fill the pupil and cover the surface of the iris. The cells form fibrous tissue, and the number of nuclei diminishes, only a few spindle-shaped cells eventually persisting between the dense bundles of fibres. This layer of tissue varies much in thickness, being usually thin, but occasionally very thick (Fig. 191). In the latter cases it is often arranged in definite layers, the deeper being more fibrous and less cellular than the superficial; this is due to recurrent attacks, with the deposition of fresh layers. A few blood-vessels and groups of lymphocytes often persist almost indefinitely in the fibrous tissue.

The inflammatory pupillary membrane produced by the organisation of exudate filling the pupil varies greatly in nature and consistency. It often forms an extremely delicate web, composed of embryonic connective tissue carrying a few capillaries with endothelial walls (Fig. 190). In other cases it is thick and dense, highly cellular and vascular at first, but later composed of fibrous tissue with few cells and few or no blood-vessels. All gradations between these two conditions are met with. When resulting from perforating wounds or ulcers, bands or filaments of fibrous tissue often stretch from the iris or pupillary membrane to the corneal scar, having been more or less stretched out, according to their consistency, when the anterior chamber was re-established.

Chronic Iritis

Chronic iritis assumes different forms. In its simplest form there is no exudate, but some granulation tissue or new-formed fibrous tissue. There are often thickenings of the iris in places, and here nodules are formed of aggregations of lymphocytes (*see* "Nodular Iritis"); polymorphonuclear leucocytes are generally absent. The blood-vessels show often marked changes. They are frequently surrounded by round-celled infiltration, and are themselves degenerated, showing peri- and endarteritis. The adventitia often forms a thick hyaline ring in section, and the endothelium of the intima has disappeared. Frequently the smaller vessels are blocked by the proliferation of endothelium and endarteritis obliterans, or by hyaline degeneration. Such changes are frequent in syphilitic iritis (q. v.).

In old cases of chronic iritis the iris is usually atrophic (*v. infra*).

Chronic iritis is often associated with cyclitis, and in many of these cases hyperplasia of the tissues occurs. The endothelium is much thickened, forming several layers (Fig. 199). The nuclei may be retained, but more frequently hyaline changes take place and homogeneous warty nodules are seen, such as are found on Descemet's membrane. The vessels show thickened adventitia, and often endarteritis.

Nodular Iritis

Nodular (or pseudo-tubercular) iritis includes a variety of conditions in which the common feature is the formation of nodules, produced by aggregations of lymphocytes, with or without endothelial and giant-cells. They never caseate.

Nodular clumps of leucocytes in the iris, ciliary body, and choroid are often the only microscopical evidence of sympathetic ophthalmia in either the exciting or the sympathising eye (Schirmer and others).

They also occur in chronic iritis from various causes, *e. g.* syphilis



Fig. 192.—Nodular Iritis. × 60.

Chronic irido-cyclitis following influenza. Nodular aggregation of lymphocytes near pupillary margin of iris; there were spherical hyaline globules in the stroma of this iris. Note inflammatory pupillary membrane.

(Fuchs), leucæmia (v. Michel), etc., usually some general diathesis (Fig. 192). They may here be accompanied by epithelioid and giant-cells, and Vossius describes a sort of capsule of fibrous tissue, with spindle-cells derived from the adventitia of blood-vessels.

v. Michel found microscopic nodules, with epithelioid cells, arranged along the blood-vessels, like tubercles of the pia mater. Some of these cases are probably true tubercular iritis.

The typical pseudo-tubercular nodule in the iris is caused by certain caterpillar hairs, like that found in the conjunctiva. In this case giant-cells are formed by the irritation set up by the hairs, and they are surrounded by epithelioid cells and leucocytes (*v.* p. 84).

Purulent Iritis

Purulent iritis occurs by direct infection or as a feature of metastatic ophthalmitis. It is distinguished by widespread necrosis of the tissues, affecting also the blood-vessels, with the result that extensive hæmorrhages are found.

v. Michel found a great number of bacterial thrombi in the smaller arteries in a case of septicæmia. The vessels were blocked with fibrin, pus, and masses of cocci. The veins were dilated and packed with red corpuscles, and the surrounding stroma was filled with red corpuscles.



Fig. 193.—Purulent Iritis and Cyclitis. × 55.

Perforating wound, panophthalmitis. The anterior part consists of pus and blood in the a. c. The iris is intensely congested, densely infiltrated with polymorphonuclear leucocytes, and, to the left, quite necrotic. The ciliary processes on the right below are in the same condition as the iris, and are covered by a mass of fibrin and pus, which extends into the vitreous.

Suppurative iritis is most commonly seen in specimens of panophthalmitis following perforating wounds or ulcers (Fig. 193). The organisms cannot often be demonstrated, though in other cases they are present in great numbers. They may increase after the removal of the eye, though this can seldom occur in eyes with perforation placed at once in formol. The iris is usually thickened and filled with pus-cells, which also fill the anterior chamber, so that the exact limits of the iris are masked. The pigmented stroma cells are swollen, and their nuclei stain badly. Granules of pigment are scattered throughout the tissues, being both intra- and extra-cellular; they are aggregated into irregular clumps in places. The vessel-walls are much altered, the

cells being swollen and indefinite, often homogeneous. Sometimes the tissues are quite necrotic, so that the nuclei no longer stain, except those of the invading polymorphonuclear leucocytes.

v. MICHEL.—A. f. O., xxvii, 2, 1881. ULRICH.—A. f. O., xxviii, 2, 1882. SCHIRMER.—A. f. O., xxxviii, 4, 1892; and in G.-S., 2nd ed., 1900. VOSSIUS.—B. z. A., ii, 1891.

SYPHILIS

Syphilitic iritis has been investigated by v. Michel, v. Hippel, Fuchs, and others. It resembles the ordinary forms of chronic iritis, from which it cannot be distinguished microscopically. v. Miche, examined portions of iris removed by iridectomy; he found marked endarteritis of the smaller vessels, which were often blocked by the proliferated endothelial cells. The vessel-wall was homogeneous, and the cells of the adventitia had proliferated and formed a thick ring. These changes, however, are not specific, and were slight or absent in cases examined by Scherl and Bénoit. v. Michel and Fuchs described microscopic nodules, which could not be seen clinically. Fuchs found the iris of normal thickness, infiltrated with round-cells, chiefly in the anterior limiting zone. The nodules usually occupy the root of the iris, and include the whole thickness; they fade off into the surrounding tissue. They often break through the anterior surface and communicate with the anterior chamber. They consist chiefly of mononuclear cells embedded in a fine reticulum. Fuchs found typical giant-cells, but no caseation. There were wide capillaries inside the nodules, which differ thus from the non-vascular tubercle nodules.

This and the similar condition described by Baas may be of the condylomatous type, but it is usually impossible to distinguish condylomata from gummata (*see* "Ciliary Body"). Bärensprung considered simple syphilitic iritis to belong to the secondary stage, the nodules being gummatous (iritis gummosa). Widder, from clinical considerations, thought that nodules were frequent in the secondary stage (iritis condylomatosa or papulosa), and that true gummata, although they occurred, were extremely rare. It is noteworthy that the "condylomatous" nodules are found in the sites which are also favoured by gummata. Fuchs considers that microscopic nodules are almost constant in syphilitic iritis.

Gumma of the iris is usually solitary, and forms a yellow or brownish-red tumour with few vessels visible upon it, thus differing from typical sarcoma of the iris. It occurs by preference at the pupillary or the ciliary edge, and generally sets up comparatively little inflammatory reaction. Virchow and Billroth record the first anatomical examination. The tumour was removed from a child aged one year, and consisted of granulation tissue with giant-cells and some fatty degeneration; it was possibly tubercular. Colberg found masses of round-cells, with many new-formed capillaries, in a gumma removed by iridectomy. Similar results were recorded by v. Hippel and Neumann.

More recently gummata of the iris have been examined by Scherl,

Bénoit, and Rumschewitsch, whilst more extensive tertiary syphilitic disease of the uveal tract has been described by Baas, Hanke, Fialho, and de Schweinitz. Scherl's case was distinguished by extensive caseation and necrosis, the iris tissue having disappeared and been replaced by inflammatory deposits, the cells of which had broken down into granular *débris*, which also pervaded the anterior chamber. In Bénoit's case there was also much destruction of tissue, with the production of a cavity which contained a few pus-cells. Surrounding this was tissue containing giant-cells, epithelioid and round cells, and pigment granules. The giant-cells were partly of the Langhans type, the nuclei being arranged around the pheriphery; in others the nuclei were central. In the anterior part of the tumour were many new-formed blood-vessels, consisting of endothelial tubes with wide lumina. Some of the iridic vessels were obliterated by endarteritis.

Rumschewitsch's case, unlike the others, occurred definitely in the tertiary stage. The gumma was oval, 3 mm. in diameter. The centre was structureless apart from a few fine granules; it did not stain, and the periphery stained only faintly. It was separated from the lens capsule by a thick layer of irregular pigment granules. At the periphery there were small cells, and there was a capsule around the tumour consisting of concentrically arranged spindle-cells. A little below the surface the intercellular substance was hyaline. Degenerated and obliterated vessels could be made out at the periphery best in specimens stained with thionin and eosin. There were no giant-cells.

Similar descriptions are given by Baas, Hanke, and Fialho (*v. infra.*).

VIRCHOW AND BILLROTH.—*See* v. GRAEFE, A. f. O., vii, 2, 1860. A. GRAEFE AND COLBERG.—A. f. O., viii, 1, 1861. v. HIPPEL.—A. f. O., xiii, 1, 1867. *WIDDER.—A. f. O., xxvii, 2, 1881. MICHEL.—A. f. O., xxvii, 2, 1881. FUCHS.—A. f. O., xxx, 3, 1884. BARLOW.—Trans. Path. Soc., xxvii. LIEBRECHT.—K. M. f. A., xxix, 1891. SCHERL.—A. f. A., xxv, 1892. *BAAS.—A. f. O., xlv, 3, 1898. BÉNOIT.—A. d'O., xviii, 189 RUMSCHEWITSCH.—K. M. f. A., xli, 1903. HANKE.—A. f. O., xlviii, 1899. FIALHO.—A. f. O., lii, 3, 1901. DE SCHWEINITZ.—Ophth. Rev., xix, 1900.

TUBERCLE

Tubercle of the iris occurs in three chief forms:

1. *Miliary tubercle*, characterised by a variable number of yellow nodules; it is often relatively benign, including Leber's group of cases of *attenuated tubercle*.

2. *Confluent or conglomerate tubercle*, characterised by definite tumour formation, composed of various forms of granulation tissue, which invades a greater or less part of the anterior chamber, tends to increase rapidly and destroy the eye, as well as leading to general dissemination.

3. *Tubercular iritis*, usually indistinguishable clinically from other forms of chronic iritis, *e. g.* syphilitic, but sometimes distinguished microscopically by the nature of the infiltration, the presence of tubercle systems and tubercle bacilli, and experimentally by inoculation results.

The first two groups were differentiated by Haab (1879); the third includes cases first described by Costa Pruneda (1880), and Edmunds and Brailey (1881). Gradenigo (1869) and Berthold (1871) first re-

ported cases of tubercle of the iris, giving microscopical examinations; Perls (1872) gave a good clinical description. Saltini (1875), Manfredi (1876), Baumgarten (1877), Weiss (1877), and Angelucci (1877) followed with new cases; and Haensell (1877), Cohnheim (1879), and v. Michel (1881) investigated the subject experimentally. Since then numerous papers have appeared, the most important of which will receive mention.

In *miliary tubercle* of the iris nodules are scattered over its surface in varying numbers, usually at a little distance from the pupillary edge, near the circulus arteriosus minor, or in the angle of the anterior chamber. In each case there is a tendency for the iris to be most affected in the lower part (Angelucci, Zimmermann, Schultze). The



FIG. 194.—TUBERCULAR IRITIS. × 10.

From a specimen sent by Prof. Fuchs. The iris is thickened by granulomatous infiltration. Note the deep parenchymatous infiltration of the cornea (tubercular interstitial keratitis). This consists of dense infiltration of the deep lamellæ with leucocytes; Descemet's membrane is split up and ruptured.

nodules are usually yellow, and it is by no means uncommon for them to have vessels upon the surface. As they grow and fuse they become greyish red; they may fill the whole posterior part of the anterior chamber (Fig. 194), invading the ciliary body and corneo-scleral margin. The cornea becomes infiltrated in its deeper part, showing a tubercular type of interstitial keratitis (*v.* p. 191), and may contain tubercle systems. The corneo-scleral margin may be perforated (Fig. 195), in which case phthisis bulbi usually supervenes slowly (Haab). In these severe cases general dissemination may take place, the patient dying of miliary tuberculosis.

The prognosis, however, is not necessarily bad. In many cases the nodules grow very slowly, and eventually undergo complete absorption.

These cases constitute Leber's *attenuated tubercle;* they are often improved by iridectomy, whereas this operation fails completely in other cases. Leber considers that the relatively benign course is due either to attenuated virulence of the bacilli, to the presence of an unusually small number, or to a specially strong reaction on the part of the organism; which factor is the most potent it is impossible to say. The cases may run a benign course for a prolonged period and then suddenly become more acute. Samelsohn quotes a case in a boy of six, in which miliary tubercles of the iris disappeared entirely, but were shortly after followed by pericorneal injection, meningitis, and death. In another case miliary tubercles disappeared, and were followed by the conglomerate type and tubercular meningitis, ending fatally. The same author demonstrated the relative immunity of a certain number of rabbits when inoculated with generations of the same strain of tubercle, whilst the virulence was found to increase for the majority of the animals.

In *confluent or conglomerate tubercle* there is a definite yellowish-white tumour upon the iris, though smaller nodules may also be present, often in the form of satellites around the larger mass. The growth has the usual tubercular structure, consisting of giant-cells with epithelioid and round cells surrounding them, as in Swanzy's case; there is generally extensive caseation, in which remnants of giant-cells may be made out. The individual nodules, which together make up the tumour mass, are united by bands of dense lymphocytic infiltration. The intermediate tissue is extremely vascular (Rüter). Frequently the growth increases until it fills the anterior chamber (Schell, Wadsworth, Sandford, etc.).

This type of tubercle of the iris has been well investigated by Liebrecht. Wagenmann first pointed out that growth is almost invariably forwards, and Lagrange emphasises the fact that the ciliary muscle is rarely invaded, so that the supra-choroidal space is protected. Hence perforation usually occurs at the angle before the choroid or vitreous are implicated (Fig. 195). The extra-bulbar mass continues to grow for a time, but soon caseates and may shrink; the whole eye may also shrink, as the result of the perforation (Liebrecht).

Tubercular iritis, i. e. chronic iritis due to tubercle, is generally considered to be the rarest manifestation of the disease in the iris. Examples are found in the cases of Costa Pruneda, Edmunds and Brailey, Knaggs, Kalt, and others. v. Michel's observations (*v.* p. 294) must be borne in mind when estimating the rarity of the condition. There is usually diffuse infiltration of the iris, with great thickening; there are usually many giant-cells present, but typical tubercle systems are less common than in other forms. Necrosis occurs later, and the anterior chamber is sometimes filled with material resembling pus (*e. g.* Edmunds and Brailey's case).

The demonstration of tubercle bacilli in tissues is seldom easy, and the iris forms no exception to the rule. They are usually to be found in small numbers after prolonged search; occasionally they are present in large numbers (Lagrange). The most certain test of the nature of the disease is afforded by inoculation of the rabbit's or guinea-pig's anterior chamber with a portion of the material; but even this may fail, as in a case recorded by Haensell and confirmed by Leber.

Experimental tubercle of the iris was first studied by Haensell and Cohnheim, subsequently by v. Michel and many others. Cohnheim showed that tubercular material introduced into the anterior chamber led to tuberculosis of the iris, usually followed by general infection. The latent period varies greatly—from a few weeks to several months. v. Michel examined tubercle of the iris induced in rabbits by inoculation with caseous bronchial glands, etc. He found the endothelium raised when the tubercles were superficial, but unaltered when they lay deeper in the stroma. Giant-cells were not common, but when they occurred they were surrounded by concentric layers of epithelioid cells. Near the nodules were often exudates and clumps of pigment, and proliferation of endothelium was more or less general throughout the iris. The



FIG. 195.—TUBERCULAR IRITIS. × 8.

From a specimen sent by Prof. Fuchs. There is a typical tubercle near the pupillary margin of the iris on the right. On the left the iris has prolapsed through a tubercular perforation at the limbus. It forms a huge granulomatous mass outside the globe.

anterior chamber contained a fibrinous coagulum, with leucocytes in the meshes.

Much discussion has arisen as to whether tubercle of the iris is *primary or secondary*. Many authors, including Leber, Fuchs, and de Wecker consider it invariably secondary to some focus elsewhere in the body. Cases in which intra-ocular tuberculosis has been considered primary have been reported by a great number of authors, including Parinaud (1879), Samelsohn, Poncet, Alexander, Lawford, Bach, etc., and the view that it is generally primary has been ably upheld by Denig. This author gives six tables: (1) 38 cases in which there was no tuberculosis before, and in which the patients were otherwise absolutely healthy at the time of the ocular affection; (2) 14 cases with

a tubercular history, but healthy before and during the attack; (3) 3 cases with earlier signs of tubercle, healthy at the time of the attack; (4) 17 cases of ocular tuberculosis coinciding with tuberculosis in other organs; (5) 9 cases which succumbed to general infection; (6) 10 cases in which the patients remained healthy after the disappearance of the ocular affection. Denig found only 5 cases of ocular metastasis in 60 cases of tuberculosis of the lungs, 90 of the bones and joints, 20 of the lymphatic glands in other parts of the body. These results are confirmed by statistics of tubercle of the bones collected by König. In 72 cases of tubercle of the conjunctiva there were no other signs of the disease in 52. According to Denig, therefore, tubercle in the eye resembles that in the lungs and bones in being often the primary seat of the disease; moreover metastasis, as also in these organs, is relatively rare. The question is obviously one of extreme importance as a guide to treatment.

On the other hand, the occurrence of cases of metastatic tubercle of the uveal tract can scarcely be doubted, and is probably by way of the blood-vessels. The primary seat in these cases is the lungs or bronchial glands, more rarely the peritoneum. The difficulty of eliminating such sources of infection clinically is often very great.

HAAB.—A. f. O., xxv, 4, 1879. v. MICHEL.—A. f. O., xxvii, 2, 1881. GRADENIGO.—Ann. d'Oc., lxiv, 1870. BERTHOLD.—Ann. d'Oc., lxvi, 1871. PERLS.—A. f. O., xix, 1, 1872. SALTINI.—Ann. di Ott., iv, 1875. MANFREDI.—Ann. d'Oc., lxxviii, 1876. *WEISS.—A. f. O., xxiii, 4, 1877. ANGELUCCI.—Ann. d'Oc., lxxxii, 1879. HAENSELL.—A. f. O., xxv, 4, 1879. COHNHEIM.—Die Tuberculose vom Standpunkte der Infectionslehre, Leipzig, 1879. ZIMMERMANN.—A. f. O., xli, 1, 1895. SCHULTZE.—A. f. A., xxxiii, 1896. LEBER.—B. d. o. G., 1890, 1891, 1893. SAMELSOHN.—B. d. o. G., 1893. SWANZY.—T. O. S., ii, 1882. HILL GRIFFITH.—T. O. S., x, 1890. RÜTER.—A. f. A., x, 1881. SCHELL, WADSWORTH.—Tr. Amer. O. S., 1883. SANDFORD.—T. O. S., xiv, 1894. LIEBRECHT.—A. f. O., xxxvi, 4, 1890. COSTA PRUNEDA.—A. f. O., xxvi, 3, 1880. EDMUNDS AND BRAILEY.—T. O. S., ii, 1882. KNAGGS.—T. O. S., xii, 1892. KALT.—Soc. de Biologie, 1893. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. PARINAUD.—Soc. de Chirurgie, 1879. DEUTSCHMANN.—A. f. O., xxvii, 1, 1881. PONCET.—Soc. de Chirurgie, 1882. ALEXANDER. C. f. A., viii, 1884. LAWFORD.—R. L. O. H. Rep., xii, 2, 1888. BACH.—A. f. A., xxviii, 1894. *DENIG.—A. f. A., xxxi, 1895 (Bibliography). ANDREWS.—T. Am. O. S., 1896.

LEPROSY

Isolated nodules do not occur in the iris in leprosy (Lie), but there is general infiltration with leucocytes and bacilli, the infection being secondary to that of the ciliary body. When fully developed the condition much resembles tubercular iritis. The iris is enormously thickened with granulation tissue containing clumps of bacilli, and this partially or completely fills the anterior chamber. The condition is distinguished from tubercle by the masses of bacilli, mostly arranged like bundles of cigars, the thrombosis of lymphatics by bacilli, and the absence of typical tubercle systems and caseation, though isolated giant-cells may occur (Franke and Delbanco).

PONCET.—Progrès médical, 1888. JEANSELME AND MORAX.—Ann. d'Oc., 1898. (*See* BIBLIOGRAPHY of LEPROSY under "Lids," "Cornea.")

DEGENERATIONS

Atrophy

Atrophy of the iris is the result of repeated attacks of acute or subacute iritis, of chronic iritis, glaucoma, and other conditions which lead to degenerative changes in the eye. Reference has already been made to the formation of new fibrous tissue upon the surface of the iris as the result of the organisation of exudates in plastic iritis. This tissue, by its contraction, leads to pressure and tension in the neighbouring stroma, the cells of which degenerate, first losing their long ramifying processes,

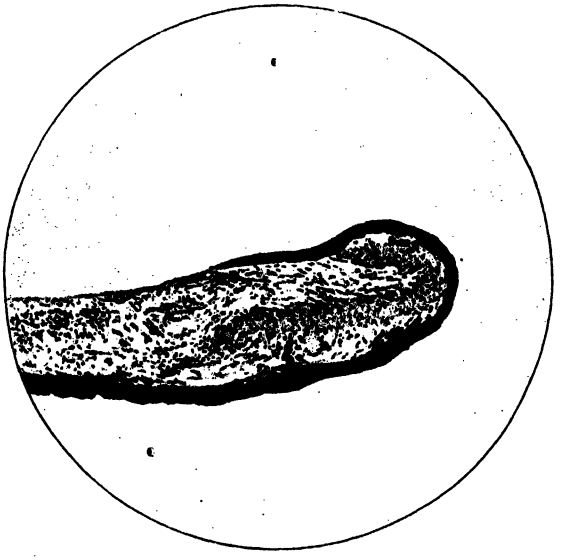


Fig. 196.—"Ectropion of Uveal Pigment."
Photograph by Lister, showing ectropion of the retinal pigment epithelium and of the sphincter iridis.

and finally atrophying in large numbers entirely. The contraction of a superficial lamina of fibrous tissue also leads to deformation of the iris. The pupillary border of the iris is pulled outwards, so that the iris becomes bent upon itself. In this manner the retinal pigment layer is dragged for a variable distance over the anterior surface, and the condition known as *ectropion of the pigment layer* is produced (Lawford, Nettleship). This is particularly common in glaucomatous eyes (Knies, Birnbacher and Czermak) (Fig. 196). When the distortion is more pronounced the sphincter takes part in the process, so that it appears hook- or horseshoe-shaped in radial section.

In the majority of cases which are examined microscopically the iris is uniformly degenerated and thinned, and this is most obvious at the root, where the iris is normally thinnest. All parts of the structure

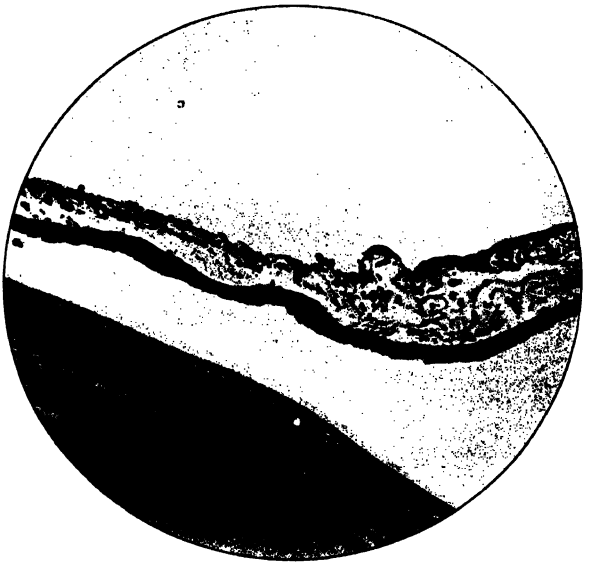


FIG. 197.—ATROPHY OF THE IRIS. × 60.

From a case of absolute glaucoma. The iris is quite atrophic. Near the surface to the left is the sphincter iridis. The blood-vessels are scarcely visible, and the stroma is reduced to a few straggling, unequally pigmented chromatophores, with a few wandering cells.

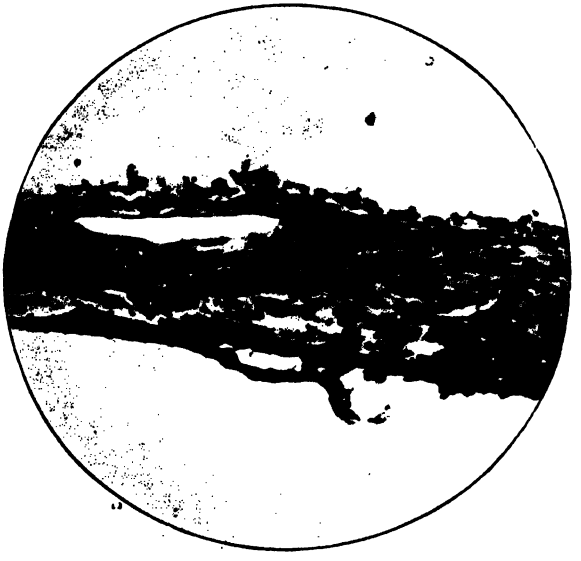


FIG. 198.—NEW-FORMED VESSEL ON THE IRIS. 140.

Holmes Spicer and Parsons, T. O. S., xxii.

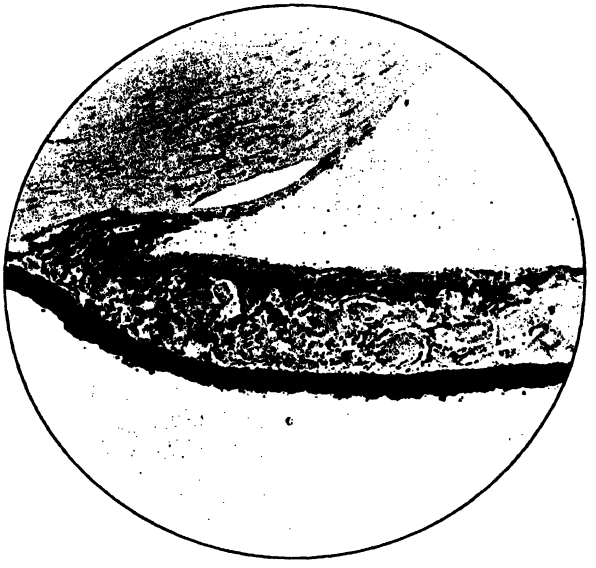


FIG. 199.—INFLAMED ATROPHIC IRIS. × 60.

From a blind painful eye with ciliary staphyloma. The figure shows the false angle of the anterior chamber. Note the hyperplasia of endothelium on surface of iris and the dilated blood-vessels, full of red corpuscles.

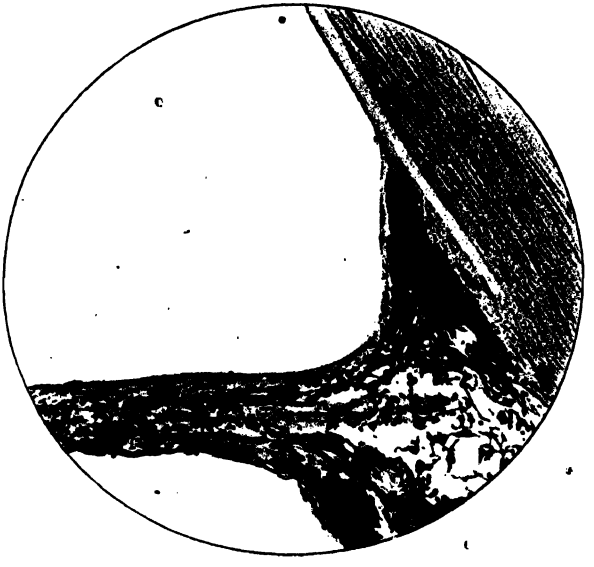


FIG. 200.—HYALINE MEMBRANE ON IRIS. × 120.

Old anterior synechia. Descemet's membrane appears to split, one branch passing over the surface of the iris. Note that it is covered by a single layer of endothelium. The iris is degenerated and densely pigmented.

participate in the process. The normal loosely constructed stroma may retain its spongy nature, though it is obvious that much of the tissue has disappeared (Fig. 197). More commonly the loose stroma is replaced by denser fibrous tissue containing flattened cells with stunted processes, and often clumps of pigment. Most of the chromatophores have been replaced by these non-pigmented cells. The muscle-fibres persist longer, so that the sphincter is generally easily recognised, though also degenerated, and more or less replaced by hyaline connective tissue. The blood-vessels often show a high degree of peri- and end-arteritis (Ulrich), sections showing the usual picture of thick hyaline rings enclosing a minute lumen, which may contain pigment. In other cases scarcely any vessels are to be seen, and sometimes the largest of these are obviously vessels of inflammatory new formation (Fig. 198). In many cases spherical hyaline globules, staining deeply with eosin, are seen in the intercellular spaces. They often



FIG. 201.—HYALINE PUPILLARY MEMBRANE AND ANTERIOR SYNECHIA. × 60.

Pannus degenerativus, thinning, and interstitial infiltration and vascularisation of the substantia propria. A fine fibrous anterior synechia is covered by endothelium, which has passed on to the iris and over the pupillary area, subsequently producing a complex folded hyaline membrane.

occur in the iris in anterior staphylomata (Sachsalber) in conjunction with hyaline changes in the cornea. The globules, which vary in size and sometimes form considerable concretions which may later calcify, are scattered throughout the stroma, and even in the endothelium and pigment epithelium.

The pigment epithelium is very resistant, but also shows degenerative changes. It may be uniformly thinned, but more often is irregular—thin or absent in places, whilst aggregated into clumps elsewhere. In high degrees of atrophy it has almost entirely disappeared; it is in such cases that a red reflex is obtained through the iris with the ophthalmoscope, and I have seen this condition in a severe case of retinitis pigmentosa.

The endothelium may be unaltered, but is often very much thickened (Fig. 199). Warty outgrowths may be formed like those upon Descemet's membrane. The cells may be well formed, with well-stained nuclei, but more frequently they are degenerated, possessing few or no nuclei,

being transformed into hyaline masses. A common phenomenon, first described by Wagenmann, is the formation of a hyaline membrane upon the surface of the iris (Fig. 200). It occurs generally in glaucomatous eyes, in which there is a peripheral anterior synechia. At the false angle Descemet's membrane is continued over the iris, or appears to split; the endothelium is similarly continued from the back of the cornea on to the new hyaline membrane, and may even pass over the pupillary border on to the pigment epithelium at the back of the iris. The hyaline membrane is usually thin (5—6 μ), but may have warty excrescences; it is doubtless a secretion product of the endothelial cells.

LAWFORD, NETTLESHIP.—T. O. S., vi, 1886. KNIES.—A. f. O., xxii, 3, 1876. BIRNBACHER AND CZERMAK.—A. f. O., xxxii, 2, 1886. ULRICH.—A. f. O., xxviii, 2, 1892; xxx, 4, 1884. WAGENMANN.—A. f. O., xxxviii, 2, 1892. GEPNER.—A. f. O., xxxvi, 4, 1890. HARING.—A. f. O., xliii, 1, 1897. SACHSALBER.—B. z. A., xlviii, 1901. FRANCK.—A. f. A., xlvii, 1903.

CALCAREOUS DEGENERATION AND OSSIFICATION

We have already seen that calcareous deposits sometimes occur in the atrophic iris. Rarely bone lamellæ are found, but almost invariably they are formed by extension from bony deposits in the choroid. Panas described a case which he regarded as primary; the iris was found to be bony in a man of thirty-six, upon whom an iridectomy was being performed. Microscopic examination of the fragments removed demonstrated the presence of osteoblasts.

PANAS.—Gaz. des Hôpitaux, 1868.

THE ANGLE OF THE ANTERIOR CHAMBER

Abnormalities in the angle of the anterior chamber occur in a large variety of pathological conditions, and present many different appearances in microscopical sections. Of these the commonest and most important is the obliteration of the true angle by the adhesion of the peripheral part of the iris to the cornea over a less or greater area (Figs. 203—5). This is the condition found in the great majority of cases of secondary glaucoma. Its importance was first insisted upon by Knies and Weber, working independently in 1876, and following a clue given three years earlier by Leber.

The earliest phase of obliteration of the angle is found in simple apposition of the periphery of the iris to the cornea, brought about by the physical conditions which induce the onset of the glaucoma, and which will be fully considered in discussing the general pathology of this disease. The iris under these circumstances may be normal or inflamed; in the latter case exudates are thrown out which rapidly lead to actual adhesion, and this follows in any case if the apposition is sufficiently prolonged. Here the irritation induced, while insufficient to produce the more marked anatomical characteristics of inflammation,



FIG. 202.—NORMAL ANGLE OF ANTERIOR CHAMBER. 34.

From a specimen by Lister. The eye was normal apart from extensive pigmentation of the conjunctiva and epithelium of the cornea. There are a few scattered pigment-cells upon the ligamentum pectinatum iridis. Schlemm's canal normal.



FIG. 203.—PERIPHERAL ANTERIOR SYNECHIA. × 55.

Secondary glaucoma from detached retina following a blow. 27, I, 1900, blo 11, ix, 1900, detached retina seen; 24, iii, 1902, inflammation, T + 2. Narrow peripheral anterior synechia; the adherent iris is more degenerated than in Fig. 204. Schlemm's canal is open, but surrounded by infiltration.

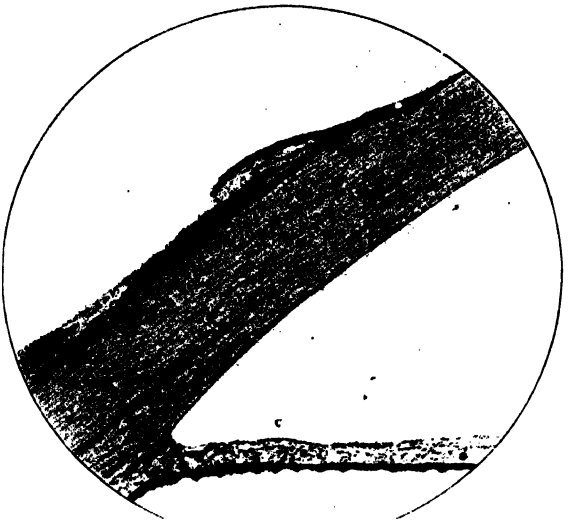


FIG. 204.—PERIPHERAL ANTERIOR SYNECHIA AND PTERYGIUM. × 25.

Narrow peripheral anterior synechia in glaucoma of four months' duration. The iris is commencing to degenerate. *See also* Fig. 54.

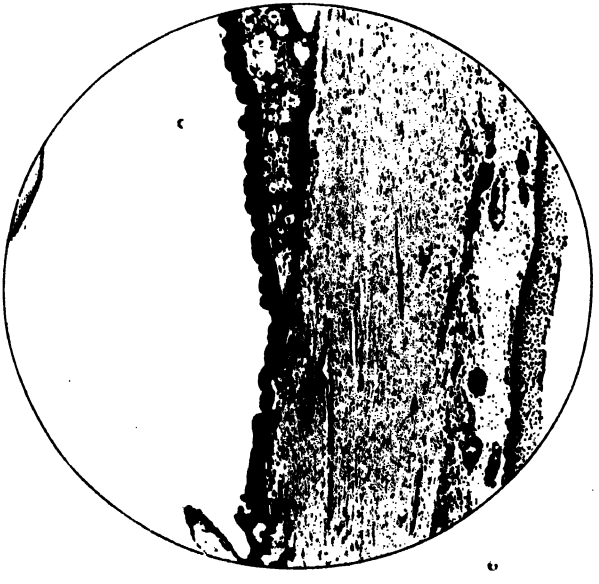


FIG. 205.—PERIPHERAL ANTERIOR SYNECHIA. × 55.

Old glaucoma; extensive peripheral anterior synechia, with almost complete atrophy of part of adherent iris. The iris elsewhere is degenerated; note hyaline degeneration of walls of vessels. Schlemm's canal infiltrated.

leads to proliferation of the endothelium of Descemet's membrane and of the iris, with fusion of the two layers. The endothelium subsequently disappears except at the false angle, where it is often heaped up. There is usually round-celled infiltration of the deeper layers of the cornea and sclera, most marked around the canal of Schlemm, which may be completely masked. The fixed tissue cells proliferate later, giving rise to young connective-tissue cells and fibres, which permanently bind the iris firmly to the corneo-sclera. The further changes which ensue are mostly degenerative in character. The endothelium of the ligamentum pectinatum atrophies, and its fibres become incorporated in the new fibrous tissue. Organisation also occurs around Schlemm's canal, which becomes partially or completely obliterated. The iris stroma atrophies gradually, being represented only by a thin layer of fibrous tissue between the corneo-sclera and the retinal pigment epithelium, which itself finally becomes thinned, and may disappear in parts. The pigment often migrates into the neighbouring tissues, being especially prone to follow the prevailing lymph-stream, so that it becomes deposited in clumps around the perforating anterior ciliary vessels. Descemet's membrane also atrophies, but often extends for a short distance beyond the false angle. The endothelium here and over the iris may gradually secrete a new hyaline membrane so that Descemet's membrane appears to split at the new angle (*v.* p. 304). Degenerative changes simultaneously occur in the whole iris, which assumes all the characteristics of an atrophic iris.

Obliteration of the angle may be partial at first, so that the whole circle must be examined before the full extent can be definitely demonstrated. Other pathological changes are usually present where the angle is open. As already mentioned, obliteration may occur in the absence of typical iritis. In these cases proliferation of endothelium is first seen, followed by formation of new connective tissue. The latter, as it contracts, approximates the iris to the corneo-sclera, and leads to an effectual fusion of the two. This process has been compared by Ziehe and Axenfeld to the proliferation of the endothelium of lymphatics in chronic hyperæmia with increased lymph-flow. The same process occurs at the edges of a partial obliteration of the angle, so that there is a continual gradual increase in extent, and ultimately the whole circle is completed. Moreover, the local peripheral anterior synechia doubtless acts as an irritant to the iris, causing deleterious abnormal stress and strain during the perpetual movements of the iris. Hence an irritable condition is induced, which is easily lit up into a definite iritis by slight exciting causes, and each exacerbation increases the area of obliteration.

The efficiency of the filtration angle is impaired by many conditions, and several of these manifest themselves anatomically apart from actual peripheral anterior synechia. It is well known that in irido-cyclitis the aqueous contains more proteid than normal, in spite of the almost complete absence in some cases of formed elements, such as leucocytes, etc. This condition may manifest itself in sections by the presence of granular deposits in the anterior chamber, especially at the angle and on the bounding surfaces. In most cases these deposits are



FIG. 206.—ANGLE IN PANOPHTHALMITIS. × 10.

Purulent iritis and cyclitis. The iris is covered with a fibrinous coagulum containing polymorphonuclear leucocytes, which are most numerous in the angle of the a. c.



FIG. 207.—PERFORATING WOUND—PANOPHTHALMITIS. × 7.

The cornea is densely infiltrated throughout with leucocytes; the a. c. is full of pus-cells enmeshed in a network of fibrin. The dark mass in front of the iris on the right is an hyphæma. The iris, lens, and ciliary body lie in a bed of fibrin, leucocytes, and red corpuscles.



FIG. 208.—CHOLESTERIN IN ANTERIOR CHAMBER. × 55.

Irido-cyclitis following injury five years before excision; T −. A. c. full of fibrinous coagulum containing leucocytes, pigment-cells, free pigment granules, calcareous granules, and cholesterin. The linear white spaces show where cholesterin crystals have been dissolved out. Note the new fibrous tissue, with very few nuclei, on the surface of the iris; Descemet's membrane appears to split, sending a hyaline membrane on to the surface of the fibrous lamina.



FIG. 209.—PIGMENT IN ANGLE OF ANTERIOR CHAMBER. × 55

Irido-cyclitis following a blow. The angle is open, but the ligamentum pectinatum is covered and infiltrated with leucocytes and pigment-cells; most of the latter are leucocytes containing pigment granules.



FIG. 210.—PIGMENT IN ANGLE OF ANTERIOR CHAMBER. × 55.

From the same specimen as Figs. 173, 174. The ligamentum pectinatum iridis is densely packed with pigmented cells, and there are great clumps of pigment in the iris. The pigment gave the reaction for iron.



FIG. 211.—PIGMENT IN ANGLE OF ANTERIOR CHAMBER. × 55.

The angle is filled with a dense mass of pigmented retinal epithelium, with some leucocytes and red corpuscles. The iris is congested and necrotic, as shown by the absence of stained nuclei. There is a similar pigmented mass behind the iris. The nature of the case is doubtful; there had been an injury fourteen days before excision.

washed out during the processes of hardening and embedding. When they are retained they may show slit-like spaces from which cholesterin crystals have been dissolved out, a condition found occasionally in cases of phthisis bulbi (Fig. 208). The coagulum is often fibrinous, and may be found filling the angle and covering the limiting surfaces of the chamber, or even filling it (Figs. 206, 207). There are always cellular elements—leucocytes, red corpuscles, pigment-cells, etc.—in these cases, but they vary greatly in number and variety.

Leucocytes are often carried into the meshes of the ligamentum pectinatum by the lymph-stream. Here they are caught as in a filter, and may effectually block the spaces of Fontana. Schirmer attributes rise of tension in sympathetic ophthalmia to this agency.

Pigment-cells and clumps may also be caught in the meshes of the ligamentum pectinatum (Lawford, Priestley Smith, Panas and Rochon-Duvigneaud, Dolganoff, E. v. Hippel) (Figs. 209, 210, 211). The pigment may be derived from the iris, ciliary body, or retinal pigment epithelium, or from melanotic growths of the iris (Solomon), ciliary body or choroid (Panas and Rochon-Duvigneaud), or from blood-pigment. Hæmatogenous pigment gives the iron reaction in the early stages; moreover, it cannot be bleached by the ordinary methods applicable to autochthonous pigment. It usually occurs as granules in leucocytes. Other forms of pigment often appear as dark brown homogeneous globules, and dense aggregates of such globules are sometimes found in the angle.

Red corpuscles are frequently found in small numbers, and, of course, in large numbers in cases of hyphæma (Fig. 207).

LEBER.—A. f. O., xix, 2, 1873. KNIES.—A. f. O., xxii, 3, 1876; xxiii, 2, 1877. WEBER.—A. f. O., xxiii, 1, 1877. ZIEHE AND AXENFELD.—Vossius' Sammlung, iv, 1901. SCHIRMER.—In G.-S., 1900. PRIESTLEY SMITH.—The Pathology and Treatment of Glaucoma, London, 1891. PANAS AND ROCHON-DUVIGNEAUD.—Récherches anat. et clin. sur le Glaucome, Paris, 1898. LAWFORD.—R. L. O. H. Rep., xi, 3, 1887. DOLGANOFF.—A. f. A., xxxix, 1899. E. v. HIPPEL.—A. f. O., lii, 3, 1901. SOLOMON.—T. O. S., ii, 1882.

CYSTS

Cysts of the iris were classified by Hulke in 1867 into four groups—

(1) Delicate membranous cysts, with an epithelial lining and clear limpid contents.

(2) Thick-walled cysts, with opaque thicker contents.

(3) Solid cystic collections of epithelium, wens or dermoid cysts.

(4) Cysts formed by deliquescence in myxomata.

In the light of increased knowledge they may be most satisfactorily classified into the following groups:

(1) Implantation cysts, including pearl cysts and atheromatous cysts;

(2) Retention cysts;

(3) Congenital cysts;

(4) Cysts of the retinal epithelium;

(5) Parasitic cysts.

To these must be added complex cysts, in the formation of which not only the iris but also the cornea and anterior chamber take part. These are usually either implantation cysts or cysts of inflammatory origin. Many of the latter are not true cysts in the strict sense of the term.

Implantation Cysts

It has been shown in the case of the skin that particles of the superficial epidermis can be transplanted into the subcutaneous tissue, and will often grow there, forming small epithelial tumours. These have been called epithelial pearl tumours (Virchow), cholesteatomata (Müller), or epidermidomata. They occur also as the result of injury, *e.g.* pricks with a needle, or, in cattle, prods with an iron spike (Bland-Sutton). We have seen that they also occur in the cornea as the result of injury or operation (p. 253). Sometimes the epithelium is carried deeper, and is implanted into the iris. It may then grow at any part, but most frequently near the periphery. Not infrequently eyelashes are carried into the anterior chamber; the epithelium of the root-sheath may then become implanted and give rise to pearl tumours or cysts (Figs. 212, 213).

The possibility of these implantations has been proved experimentally by various investigators. Dooremaal (1873) introduced inert foreign bodies and living tissue into the iris of dogs and rabbits, and succeeded in obtaining grafts. Goldzieher (1874) obtained an epithelial cyst from a fragment of nasal mucous membrane. Schweninger (1875) implanted hairs into the anterior chambers of dogs and rabbits. Masse (1881) most exhaustively investigated the subject. The graft undergoes a certain amount of absorption and becomes white; later it may become vascularised. Masse kept rabbits for eight months with such grafts. He also grafted skin containing hairs. Microscopically there is a thick layer of stratified epithelium formed, united by connective tissue to the iris. He saw definite cystic development in the centre of such a graft, derived from the conjunctiva. In a later communication (1883) he showed that fragments of cornea might also be implanted and give rise to pearl tumours. Pieces of muscular tissue, etc., are absorbed, and do not give rise to tumours. Masse's experiments were repeated and confirmed by Hosch (1885); he showed that sebaceous glands might survive.

Mackenzie published a case of cyst of the iris, and drew attention to its traumatic origin. The relationship to injury was particularly noted by Buhl and Rothmund, with whose names the implantation theory is specially associated. Rothmund (1871) collected thirty-six cases, in which twenty-eight had a perforating wound; in three there were eyelashes in the anterior chamber; in two cysts followed cataract operations. Monoyer (1872) distinguished between the solid pearl tumours and the cysts, and threw doubt upon the traumatic origin. In one case there were two pearl tumours, the size of a millet-seed, resembling mother-of-pearl. Histologically they were composed of solid concentric lamellæ of epithelium, arranged like the layers of an onion. The

central part is often horny in these growths. Becker reported a cyst with compact walls, containing many elastic fibres, and lined with

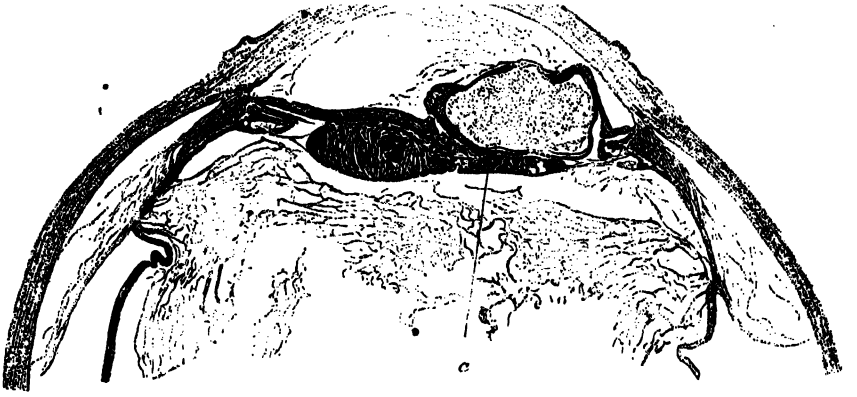


FIG. 212.—CYST OF IRIS. × 10.

From Treacher Collins. Following implantation of an eyelash. *a* is the part shown in Fig. 213. (T. O. S., xiii.)

flattened epithelium. Stölting described two epithelial cysts, and pointed out the possibility of continuity of the epithelium with that of

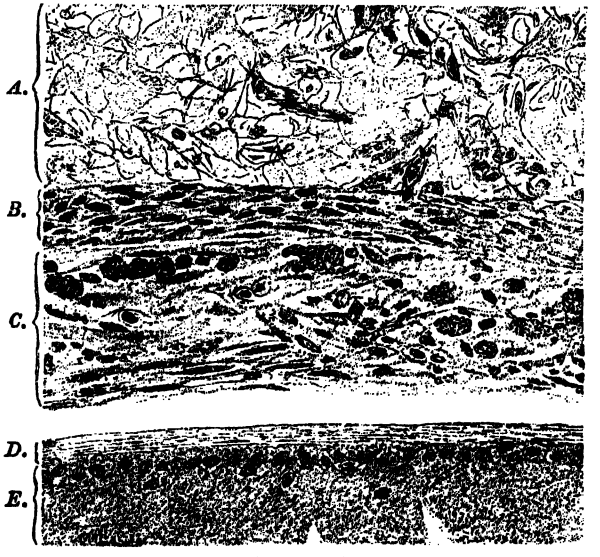


FIG. 213.—CYST OF IRIS. × 300.

From Treacher Collins. *A*, contents of cyst; *B*, epithelial lining of cyst; *C*, iris; *D*, lens capsule; *E*, lens. (T. O. S., xiii.)

the surface by downgrowth along the lips of the wound into the anterior chamber.



FIG. 214.—EPITHELIAL CYST OF THE ANTERIOR CHAMBER. × 5.

From a man, æt. 56, who had had a wound of the cornea, with prolapsed iris, two and a half years before. The cyst, 7 mm. in diameter, was situated below the cornea. It is lined with epithelium varying in the number of layers. The epithelium is continuous over the iris, fibrous tissue filling the coloboma, etc., and lines the whole anterior chamber.

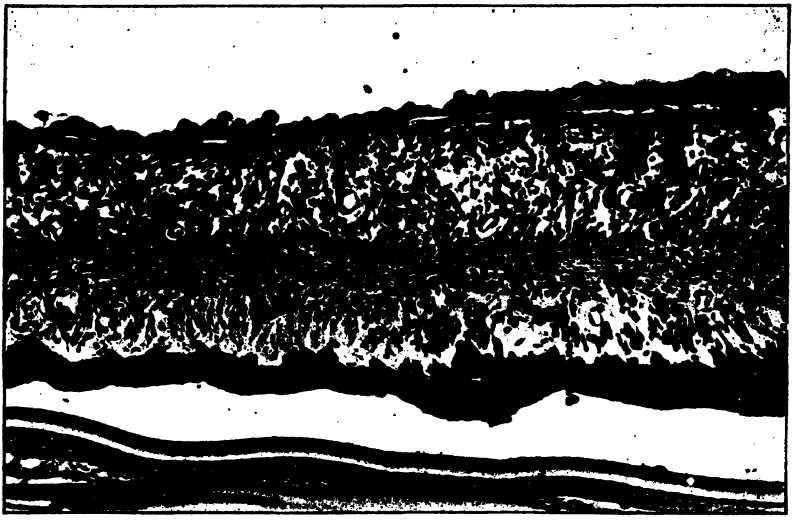


FIG. 215.—EPITHELIUM COVERING IRIS. × 130.

Four months after iridectomy; T + 2 before excision. The iris is covered by a layer of stratified epithelium which is continued across the coloboma, shutting off the posterior from the anterior chamber. There was no epithelium on the back of the cornea. The number of layers of cells varies, in places there are small cysts; the epithelium resembles conjunctival epithelium. The figure shows the sphincter iridis cut obliquely.

Wintersteiner records a small pearl tumour growing on the iris in the angle of the anterior chamber. It consisted chiefly of very fine, wavy lamellæ, without nuclei, and embedded in granulation tissue and new-formed fibrous tissue. The lamellæ were horny epithelial cells. These



FIG. 216.—CYST OF EYE.
From Treacher Collins. Large epithelial cyst in a shrunken eye. (T. O. S., xi.)



FIG. 217.—CYST OF EYE.
From Treacher Collins. Showing laminated epithelium lining the cyst in Fig. 216 (T. O. S., xi.)

acted as foreign bodies and caused the formation of many giant-cells. The whole was pervaded with chloresterin crystals.

Cases of eyelashes growing in the iris and anterior chamber have been recorded by Rockliffe, Stoeber, Pamard, Schweigger, and Cross and Collins, and others. In the last-mentioned case (Figs. 212, 213), the cyst in the iris had opaque white contents, consisting of polyhedral cells, most without nucleus. They were probably epithelial cells undergoing degeneration. There were numerous globules of fat and probably cholesterin. The cyst was lined with epithelium. This case represents a transition stage from the solid pearl tumour to the fully developed cyst.

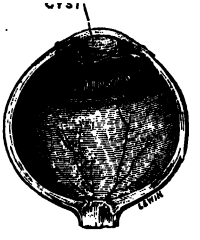


FIG. 218.—CYST OF ANTERIOR CHAMBER.
From Treacher Collins. Following cataract extraction. (T. O. S., xii.)

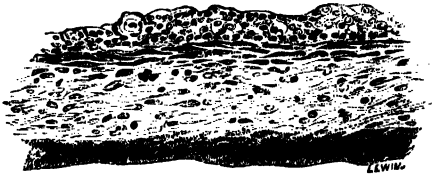


FIG. 219.—CYST OF ANTERIOR CHAMBER.
From Treacher Collins. Epithelium lining cyst shown in Fig. 218. (T. O. S., xii.)

Implantation cysts sometimes contain sebaceous material as well as hairs, as in v. Graefe's case. One recorded by Strawbridge was lined with a layer of squamous epithelial cells, swollen, and in an advanced stage of fatty degeneration. These cells were free from each other, and were surrounded by granular matter, fat, and cholesterin crystals. In

Snell's case the contents of the cyst consisted of a number of very large, clear, closely packed cells like fat-cells, in which no nucleus was discernible; of cholesterin crystals in great numbers; of a large quantity of fatty matter, both in the purely granular and oily forms; of pigment-cells and granules in small quantity; of sparsely scattered tesselated epithelium, and of a purely granular material.

More commonly the contents of the cysts are serous or slightly turbid fluid. Cases of this kind have been reported by Benson, Morton, Marshall, and others. In these the iris is often split into two layers; the anterior is often adherent to the back of the cornea, and is usually thin and atrophic. The posterior layer constitutes the greater part of the iris, and forms the posterior wall of the cyst, which is, as

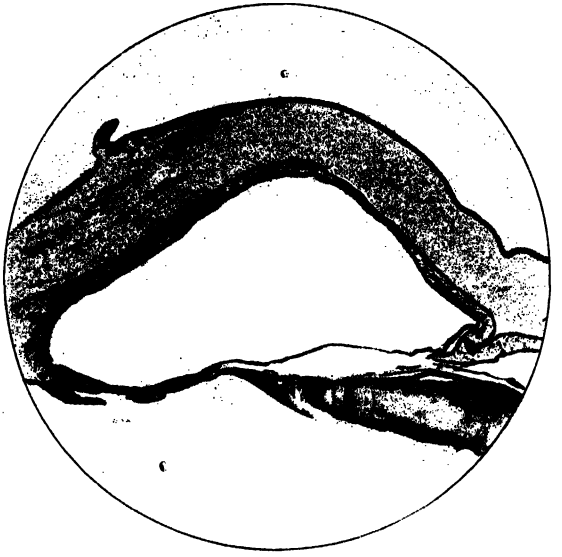


FIG. 220.—EPITHELIAL CYST OF POSTERIOR CHAMBER. × 12.
The iris is adherent to the cornea. The space bounded by iris, ciliary processes, and lens is lined by stratified epithelium.

usual, lined with irregular and often ill-developed stratified epithelium. This, where best developed, sometimes closely resembles the corneal or conjunctival epithelium, the cubical cells covering the iris, and the flattened cells lining the cavity.

Implantation cysts are often not limited to the iris, this forming only the posterior wall (Figs. 214, 216, 218). The anterior wall is then formed by the back of the cornea, an anterior synechia closing the cyst, which is, as usual, lined with epithelium. Sometimes the cyst extends on to the capsule of the lens, which forms part of the posterior wall, and it may even protrude under the conjunctiva, as in a case reported by Critchett. Often several epithelial cysts occur in the same eye, of various sizes, some being purely corneal or iridic, and others bounded by various portions of the walls of the anterior chamber.

Wintersteiner records a case in which the epithelium invaded the wounded lens and formed numerous folds in it.

The occurrence of downgrowths of the superficial epithelium into the anterior chamber, which may result in the whole or parts of the chamber being lined by stratified epithelium, must be remembered. Doubtless many so-called implantation cysts—more especially of the iris *and* anterior chamber—are due to this cause, as rightly insisted on by Stölting (*v.* p. 165).

HULKE.—R. L. O. H. Rep., vi, 1, 1869. BLAND-SUTTON.—Hunterian Lectures, R.C.S., 1889; Tumours, London, 1896. DOOREMAAL.—A. f. O., xix, 3, 1873. GOLDZIEHER.—Arch. f. exp. Path. u. Pharm., ii. SCHWENINGER.—Z. f. Biologie, xi, 1875. *MASSE.—Comptes rendus de l'Acad. des Sciences, 1881, 1883; Kystes, Tumeurs perlés et Tumeurs dermoides de l'Iris, Paris, 1885. HOSCH.—Virchow's Archiv, xcix, 1885. MACKENZIE.—Diseases of the Eye, London, 1830. ROTHMUND.—B. d. o. G., 1871; K. M. f. A., x, 1872. MONOYER.—Ann. d'Oc., lxvii, 1872. BECKER.—B. d. o. G., 1871. STÖLTING.—A. f. O., xxxi, 3, 1885. WINTERSTEINER.—B. d. o. G., 1900. TREACHER COLLINS.—T. O. S., xi, 1891. *CROSS AND TREACHER COLLINS.—T. O. S., xii, 1892; xiii, 1893. STRAWBRIDGE.—T. Amer. O. S., 1878. SNELL.—R. L. O. H. Rep., x, 1881. MORTON.—T. O. S., xiii, 1893. HANSELL.—T. Am. O. S., 1895. DEVEREUX MARSHALL.—T. O. S., xix, 1899. *LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901.

RETENTION CYSTS

Serous cysts occur in the iris, which are not lined by epithelium, and in which no history of injury can be obtained. Some of these are congenital (*v. infra*), others develop spontaneously. They are probably due to blocking of the mouths of the crypts, which become distended by the retained lymph.

Sattler considered it absolutely necessary that some foreign body, no matter how microscopic, should be incorporated in the iris in order to produce irritation, leading to increased exudation (exudation cysts). Schmidt-Rimpler advanced the view that the cysts were due to thickening and fusion of the strands which are often seen crossing the crypts. de Wecker considered that they were caused by adhesion and fusion of folds of the iris, with enclosure of aqueous fluid; this view almost demands previous injury, and does not satisfactorily explain the so-called idiopathic cysts. Eversbusch considered them due to detachment of the ligamentum pectinatum iridis, caused by injury, and hæmorrhage. The anterior and middle layers of the iris are also torn up, transudation occurs from the circulus arteriosus iridis major, and a cyst is formed in the space between the iris and cornea. Gayet published a case, examined microscopically, which supports Eversbusch's theory.

Treacher Collins has reported two cases which he regards as supporting Schmidt-Rimpler's theory. There was no history of injury. In one, which may be considered a typical case, the cyst was situated nearer the anterior than the posterior surface of the iris. It was lined with a layer of flattened endothelial cells, resting on a very distinct basement membrane. The latter was best seen on the posterior wall, and was composed of closely packed nucleated fibres.

Greeff has insisted upon the fact that retention cysts lined by

endothelium can occur after injury as well as implantation cysts. There can be no doubt that endothelium, *e. g.* that lining Descemet's membrane, can at times give rise to several layers of superposed cells, quite apart from the frequent appearance of several layers due to oblique section. It is by no means easy always to determine whether the cells are of epi- or endo-thelial origin, especially when one remembers that epithelium growing under these abnormal circumstances is often atypical.

The retention cysts are said to be always unilocular. They are often collapsed and folded when cut, so that appearances of multilocular cysts are common in sections.

SATTLER.—K. M. f. A., xii, 1874. SCHMIDT-RIMPLER.—A. f. O., xxxv, 1, 1885. DE WECKER.—Traité d'O., ii, 1886. EVERSBUSCH.—Beiträge z. Genese der Iriscysten, 1880. *TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1, 1890. GREEFF.—A. f. A., xxv, 1892. *LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901.

CONGENITAL CYSTS

A few cases of true dermoid cysts of the iris have been reported (v. Rosenzweig, Lagrange). They are practically identical microscopically with the pearl tumours or the implantation cysts, and it is doubtful in which category they should be included. v. Rosenzweig, indeed, is inclined to put the implantation cysts amongst the true dermoids. This is certainly wrong in most cases, the epithelium having but slight resemblance to epidermis, owing to the absence of prickle-cells.

Many of the retention cysts are congenital. One recorded by Clark probably originated in the spaces of Fontana. Guaita explains another on Eversbusch's theory. Both were lined with endothelium. Others by Herrnheiser, Klein, Noyes, etc., are insufficiently reported.

A remarkable congenital cyst, lined by ciliated epithelium, has been published by O. Becker and Krückow. The cyst lay in an anterior staphyloma.

Congenital cysts occur in connection with colobomata of the iris, etc., and other malformations of the eye. These will be considered elsewhere. It is possible that Becker and Krückow's case belongs to this group.

v. ROSENZWEIG.—B. f. A., xvi, 1894. *LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. CLARK.—VIII Internat. Congress, Edinburgh, 1894. GUAITA.—Ann. di Ott., x, 1881. OSBORN.—St. Thomas's Hosp. Rep., vi. O. BECKER.—Atlas, Wien., 1878. KRÜCKOW.—A. f. O., xxi, 2, 1875.

CYSTS OF THE RETINAL EPITHELIUM

Treacher Collins has shown that cysts may be formed by separation of the two layers of retinal pigmented epithelium at the back of the iris (Figs. 221—3). Small cystic spaces of this nature are of frequent occurrence in various pathological conditions. Treacher Collins records three cases. In one, in a man æt. 64, a black mass with a notch in the middle, projected from behind the lower margin of the pupil. In another, a boy æt. 10, the eye had been wounded with a pair of scissors seven years before; the posterior wall of the cyst was

adherent to a cyclitic mass of fibrous tissue and to the capsule of the shrunken lens. In the third there was no posterior synechia; there was a sarcoma of the ciliary body—"the pressure of this tumour on the base of the iris gave rise not only to œdema of its stroma, which is

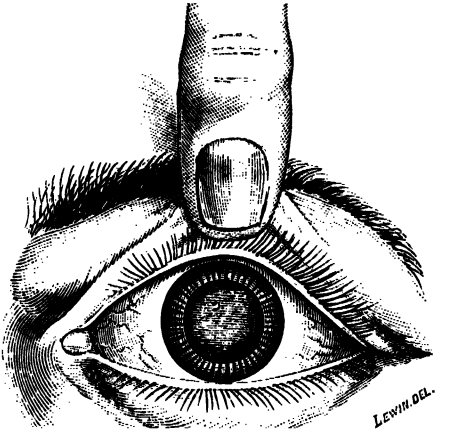


FIG. 221.—CYST OF RETINAL PIGMENT EPITHELIUM.
From Treacher Collins.

seen to be swollen, but also to effusion of fluid between its two uveal layers," and so to the formation of a small cyst not far from the pupillary border (Fig. 222). Eales and Sinclair record two such cysts in a glaucomatous eye.

These cysts are doubtless due, as suggested by Treacher Collins, to interference with the lymph-flow in the iris. This will be aided, if not caused, by adhesion of the root of the iris to the back of the cornea, and will be further increased by fusion of the posterior wall with cyclitic deposits (partial or total posterior synechia) (Fig. 223). The



FIG. 222.—CYST OF RETINAL PIGMENT EPITHELIUM.
After Treacher Collins. Small cyst between the two layers of pigment epithelium; from an eye containing a melanotic sarcoma of the ciliary body. The iris was swollen and œdematous.

accumulation of fluid is sometimes considerable, the anterior wall, with the main part of the atrophic iris, being bulged forwards. This is one cause of what may be regarded clinically as a partial bombé iris.

An extreme condition of œdema of the pigment layer, with the formation of numerous small cystic spaces, is common in *diabetes*.

Hirschberg and Snellen first pointed out that in iridectomy in diabetics the pigment is set free in the aqueous, which becomes dark and cloudy. Microscopically Kamocki found enormous swelling and sponginess of the uveal layer, which is from 0·17—0·33 mm. thick. Instead of forming two layers there are many layers of cells, which are extremely vacuolated, the pigment with the nucleus being pressed to one side of the cell. The cells do not stain with most dyes, but a few stain with hæmatoxylin, and then show a fine network of protoplasm. The posterior cells are much elongated cylinders, the anterior cubical or flat. The latter are particularly swollen and depigmented. The breaking down and fusion of the cells leads to the formation of cysts



FIG. 223.—CYSTS OF THE PARS RETINALIS IRIDIS. × 7.

From a boy, five years after injury. Seclusio and occlusio pupillæ; separation of the two layers of retinal pigment epithelium, with the formation of numerous cysts. The pupillary membrane is extremely delicate. Note the anterior capsular cataract and detached retina.

reaching a breadth of 1·5 mm. and a height of 0·8 mm.; they contain free nuclei, pigment granules, and fine, pale globules. The early stages were seen by O. Becker in cases of diabetic cataract; and the proliferation, vacuolation, and sponginess were also described by Deutschmann. The remainder of the iris is usually normal, but may show œdema (Becker) or atrophy (Deutschmann). Kako has recently confirmed the observations upon the retinal pigment layer. The condition is occasionally seen in other degenerative conditions, but is markedly influenced by the presence of sugar in the aqueous, etc.

TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1, 1890; Researches, London, 1896. EALES AND SINCLAIR.—T. O. S., xvi, 1896. ZIMMERMANN.—Ann. of Ophth., 1897. KAMOCKI.—A. f. A., xvii, 1887; xxv, 1892. BECKER.—Zur Anat. der gesunden u. kranken Linse, Wiesbaden, 1883. DEUTSCHMANN.—A. f. O., xxxiii, 2, 1887. KAKO.—K. M. f. A., xli, 1903.

Parasitic Cysts

The first recorded case of *cysticercus* in the eye was in the anterior chamber (Schott and Sœmmering, 1829). Others in this situation have been recorded by v. Graefe (1853), Hirschler (1861), Windsor (1862), Teale (1866), and others. They are extremely rare here (two in 60,000 cases, A. Graefe; one in 30,000, Förster); and in no case have they been multiple. In Krüger's case the cyst was grey and transparent, 2 mm. in diameter, implanted in the lower part of the iris by a short, very thin pedicle. It altered in shape from time to time, often rapidly. The protrusion of the head of the scolex can often be seen very well in this situation. Its presence leads to severe plastic iritis.

Schott and Sœmmering; v. Graefe.—In Sichel, Iconographie ophth., Paris, 1852. Hirschler.—A. f. O., iv, 2, 1858. Windsor.—R. L. O. H. Rep., iii, 3, 1862. Teale.—R. L. O. H. Rep., v, 1866. Krüger.—K. M. f. A., v, 1867. Kries.—A. f. O., xxiv, 1, 1878. Treitel.—A. f. A., xv, 1885. Grossmann.—Ophth. Rev., vii, 1888. Herrnheiser.—Prag. med. Woch., 1889. Prager.—Wien. klin. Woch., 1892.

Filariæ have very occasionally been observed in the anterior chamber. They do not form cysts, but may be conveniently referred to here. The species has not been determined. Mercier (1771) recorded the first case in a negress of San Domingo; the cases reported by Macnamara, Barkan, and Drake-Brockman are doubtful. The most complete observation is by Coppez and Lacompte, in a negress, æt. 2½, from the Congo. The movements of the worm produced no inflammatory reaction, but iritis set in the day after it died. It was then removed and found to be 15·2 mm. long, incompletely developed, and undifferentiated as to sex.

Macnamara.—Indian Annals of Med. Sc., viii, 1864. Barkan.—A. of O., v, 1876; A. f. A., v, 1876. *Coppez.—A. d'O., xiv, 1894. *Lacompte.—Ann. de la Soc. de Méd. de Gand, 1894. Drake-Brockman.—Ophth. Rev., 1894. Gauthier.—Ann. d'Oc., cxiv, 1895. Kraemer.—In G.-S., x, 1899.

Complex Cysts

We have already referred to complex epithelial cysts, which involve not only the iris but also neighbouring parts. More common are cystic spaces formed by shutting off portions of the anterior chamber, as the result of inflammatory adhesions of the iris to the cornea, etc. Such cases were early recorded by de Wecker, Knapp, Alt, and others. The formation of a horseshoe-shaped posterior synechia and subsequent development of a localised condition of bombé iris gives rise to a condition often indistinguishable from a cyst of the iris. Such a case, as the result of an intra-ocular foreign body, is recorded by Treacher Collins. The anterior wall was formed by the upper part of the iris, bowed forwards like a sail; the posterior by the lens capsule. Inflammatory tissue united the pupillary margin of the iris to the lens capsule internally, and the anterior of the ciliary processes to the lens capsule externally. In Alt's case the iris was adherent to the cornea except at the centre, where it passed back and formed a posterior synechia with

the lens capsule. The central space was surrounded by inflammatory tissue, lined with endothelium.

Appearances resembling these cysts are often seen in sections, but the cavity is rarely completely shut off from the rest of the anterior chamber. Only serial sections could conclusively demonstrate this, and, as far as I am aware, no case has ever been submitted to this crucial test.

DE WECKER.—Traité d'O., ii, 1886; A. f. A., i, 1869. KNAPP.—A. of O. and Otology, i, 1869. ALT.—Lectures on the Human Eye, New York, 1880.

TUMOURS OF THE IRIS

NÆVUS, MELANOMA

Congenital pigmented spots in the iris are not very uncommon. They occur in two forms—as raised spots, pigmented *nævi*, or as small circumscribed tumours, *melanomata*. v. Graefe described a case of the latter, but without histological examination. Knapp found such a growth to consist of a circumscribed development of branching and anastomosing stroma-cells, some of which were unpigmented, but most were pigmented. There was no sharp delimitation from the surrounding normal tissues.

Fuchs found that pigmented nævi usually lay in the anterior limiting layer of the iris. Here the pigment granules may be so densely aggregated that the nuclei of the cells are hidden; the individual pigment granules are often very large. The surface of the iris may project forwards at the site of the nævus, which frequently lies upon a bed of pigmented stroma-cells. The nævi are often situated near the pupillary edge of the iris. Fuchs in his first paper evidently regarded the cells as derived from the stroma, though he here too recognises the existence of pigmented spots derived from the retinal pigment epithelium.

The pigmented cells of the nævus may be round (Baas), in which case their resemblance to those of true nævus of the skin, conjunctiva, etc., is well marked. It is by no means certain, however, that true nævus occurs in this situation. As shown elsewhere (p. 129), there is a growing tendency to regard dermal nævus as a modified epithelial deposit. There is normally no epithelium near the surface of the iris; this does not, however, eliminate the possibility of an epithelial "rest," nor does it militate against the endothelial theory of congenital nævi. With the scanty material at one's disposal it would be unwise to express a dogmatic opinion as to these deposits. What may be stated with certainty is, that two types of pigmented spots are met with in the iris: (1) aggregations of branched pigmented stroma-cells; (2) aggregations of pigmented cells derived from the retinal pigment epithelium. Knapp's case is an example of the first type, Fuchs's of the second, as he has since admitted (Anargyros).

Nævi may give rise to definite tumours, which are usually relatively benign, but may be malignant. Much confusion not only in nomen-

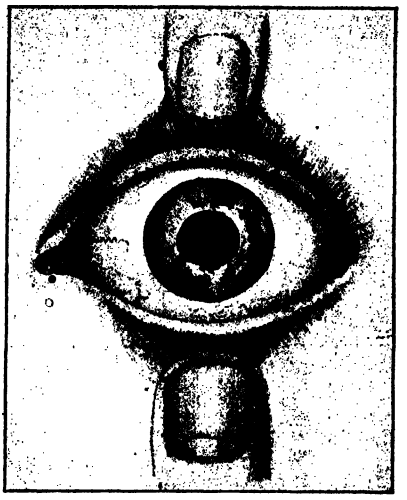


FIG. 224.—MELANOMA OF IRIS.

After Treacher Collins, R. L. O. H. Rep., xii. From a man æt. 21; there was a dark spot down and out more than four years previously.

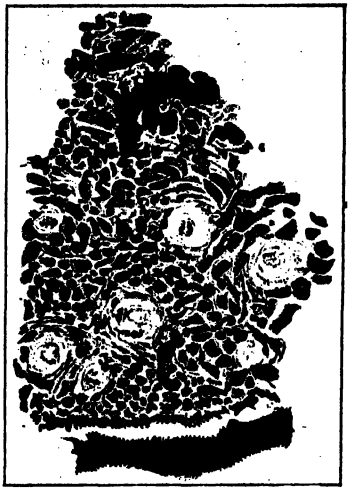


FIG. 225.—MELANOMA OF IRIS.

After Treacher Collins. From the same case as Fig. 224, showing section of lower part of iris under a high power.



FIG. 226.—HORSE'S IRIS.

After Treacher Collins. Showing the mass of pigmented epithelium at the pupillary border.



FIG. 227.—MELANOMA OF IRIS.

After Anargyros, A. f. A., xlvi. Showing clearly the relationship of the pigmented cells to the retinal epithelium.

clature, but also as to the real character of these growths has arisen. They are often classified amongst the sarcomata, and this is especially the case with the more malignant types. Those who recognise their origin from congenital nævi classify them as sarcomata or as carcinomata according to their predilection for one or other view of the nature of the nævus-cell. Others give them a separate designation, *melanomata*, and this term is often restricted to the more benign type. Fuchs divides the benign tumours or melanomata into two classes: (1) those which are due to proliferation of the pigmented stroma-cells of the iris; (2) those which occur at the pupillary margin of the iris, and are developed from the retinal epithelial cells. The first class often reach a certain size—usually quite small—and remain for many years



FIG. 228.—MELANOMA OF IRIS. × 300.
Treacher Collins, T. O. S., xix.

unchanged. They are liable at any time to take on malignant growth, and it can scarcely be doubted that the resultant tumours are rightly designated sarcomata. The second class resemble the normal outgrowths found at the pupillary margin in horses and many lower mammals (Fig. 226). These have been precisely investigated by Treacher Collins, Alt, Bayer,[1] and consist of masses of the pigmented retinal epithelium into which a few blood-vessels and a small amount of connective tissue, derived from the iris stroma, have penetrated.

Anargyros has recently given the best description of melanomata of the iris, and this shows that they are by no means limited to the pupil-

[1] TREACHER COLLINS.—Researches into the Anatomy and Pathology of the Eye, London, 1896. ALT.—Amer. Jl. of Ophth., xv, 1898. BAYER.—Handbuch d. thierärztl. Chirurgie, v.

lary margin. There were two small tumours in the upper part and one large one (1 mm. broad by 2½ mm. long) in the lower part of the pupil, besides several nævi scattered in other parts of the iris. The growths consisted of masses of deeply pigmented cells formed by proliferation of the retinal epithelium into the stroma of the iris (Fig. 227). They were situated, therefore, for the most part in the posterior layers. The individual cells were irregular in shape, and filled with very fine, round, brown pigment granules, which hid the nuclei from view. Similar outlying cells were scattered through the iris stroma. The tumour-cells were continuous with the retinal epithelium, so that the so-called Bruch's membrane ran directly into the growths.

The favourite place for melanomata is undoubtedly the pupillary margin, and this is explained by the meeting of the two layers of the secondary optic vesicle at this spot. Such places are always more subject than others to congenital malformations. The next commonest site is the neighbourhood of the peripheral edge of the sphincter, where ingrowths of the retinal pigment are not infrequent in normal eyes. The growths may lie at the extreme periphery of the iris, in such a position as to be invisible clinically (Anargyros).

Treacher Collins described a pigmented growth of the iris in a woman of sixty-three, which he regarded as a "pigment mole rather than a melanotic sarcoma." There seems no doubt that it had existed since childhood. It was composed of large endothelium-like cells, with oval, very sharply defined nuclei (Fig. 228). The cells were contained in a delicate mesh of connective tissue. Much pigment was scattered irregularly throughout the growth, being quite dense in parts and absent in other parts. Griffith regarded it as a large round-celled sarcoma.

v. Graefe.—A. f. O., vii, 2, 1860. Knapp.—Intra-ocular Tumours, New York, 1869. Fuchs.—A. f. A., xi, 1882; A. f. O., xxxi, 3, 1885; Text-book. Baas.—A. f. O., xlv, 1898. Treacher Collins.—T. O. S., xix, 1899. *Anargyros.—A. f. A., xlvi, 1902.

Angioma

Angiomata of the iris are excessively rare. In Mooren's case the growth resembled a blackberry, and bled profusely when the patient's head was shaken, the hyphæma disappearing in one and a half minutes. After dwindling to one third its former size it set up glaucoma, and was removed by iridectomy. It was not examined microscopically, and was looked upon by de Wecker as a simple granuloma.

The same explanation will apply to Schelske's case, and also to Schirmer's cavernous angioma. The latter followed a wound, was gelatinous in appearance, and speckled with hæmorrhagic spots.

Wolfe describes a tumour similar to Mooren's in a man of sixty-two, which disappeared spontaneously after seven months' duration.

Berry reports a "nævus" which involved not only the iris, but also a persistent pupillary membrane.

Alt records two cases: (1) a capillary angioma, which may have been a spindle-celled sarcoma; (2) a cavernous angioma, to which the same explanation will apply.

MOOREN.—Ophthal. Beobachtungen, 1867. SCHELSKE.—Lehrbuch, 1870. SCHIRMER.—Greifswalder med. Beiträge, iii; G.-S., iv, 1876. WOLFE.—Med. Times and Gazette, 1880. BERRY.—Diseases of the Eye, Edinburgh, 1889. ALT.—Am. Jl. of Ophth., xvii, 1900.

MYOMA

Myoma of the iris—independent of the ciliary body—has, as far as I am aware, been hypothecated in only one case. The tumour was examined by Devereux Marshall and diagnosed as a fibro-sarcoma (Fig. 229). Griffith regarded it as a myoma. No differential staining methods were employed. (*See* "Ciliary Body").

THOMPSON.—T. O. S., xix, 1899.

SARCOMA

Primary sarcoma of the iris is a rare disease. Tay (1866) reported the first case with microscopical examination. The recorded cases have been collected by Knapp (1879), Fuchs (1882), Treacher Collins (1889), Ewetzky (1896), Werther (1896), and finally by Casey Wood and Brown Pusey (1902). The last authors give abstracts of eighty-three cases in which microscopical examination was made.

Fuchs found sarcoma of the iris 16 times in 259 collected cases of sarcoma of the uveal tract, Martin 1 in 43, Lawford and Treacher Collins 1 in 103 (Moorfields cases). Twenty-seven cases occurred under, 57 over thirty years of age; 36 in males, 45 in females (Wood and Pusey). Melanotic sarcomata appear to be commoner over forty years of age, and leuco-sarcomata in young patients; but little stress can be laid upon this deduction, both on account of the small number of cases, and also because pigment is often overlooked in so-called leuco-sarcomata.

In 35 cases the primary seat of the tumour was in the lower half of the iris, in 13 in the upper half, in 5 in the inner side, and in 2 in the outer side. It sometimes occurs in both eyes (Brudenell Carter).

Sarcomata of the iris are usually melanotic. They are at first small, and in numerous cases grow for months or even years without causing vascular injection of the eye or interfering with the mobility of the iris. They are frequently nodular, and always very vascular, their vessels being often visible to the naked eye. Sometimes several tumour masses occur in the same iris; this is probably due to local dissemination by means of the aqueous- and lymph-streams, not by way of the blood. Pigmented and non-pigmented nodules may appear side by side.

There is at first no iritis, and inflammatory reaction is always slight until secondary glaucoma supervenes in the second stage of the disease. In several cases the first symptom drawing attention to the growth has been recurrent hæmorrhage into the anterior chamber; in others involvement of the pupillary area has led to interference with vision.

The tumour usually grows more quickly in the later stages, sometimes filling the anterior chamber or perforating the walls of the globe, and so leading to the third stage, that of extra-ocular growth. This is

usually brought about by invasion of the ligamentum pectinatum, ciliary body, and the walls of Schlemm's canal; the cells then grow along the perforating anterior ciliary vessels and appear externally upon the anterior part of the sclerotic, and therefore, unlike tubercle of the iris, somewhat posterior to the limbus. Early and extensive involvement of the ciliary body often renders it impossible to decide the primary seat of the growth. Lateral and posterior dislocation of the lens often occurs, especially in growths starting in the posterior layers of the iris.



FIG. 229.—MYOMA (?) OF IRIS. × 200.
Thompson, T. O. S., xix.

The fourth and final stage is the general dissemination of the disease in other organs of the body, almost invariably by way of the blood-stream.

Microscopically sarcoma of the iris is a diffuse growth, and is rarely and only relatively circumscribed. In this respect it differs from the benign melanoma, but the difference may be deceptive. At the same time it almost invariably forms a definite tumour, the infiltrating or flat type of sarcoma having been described only as a secondary growth in the iris (*see* "Ciliary Body").

The cells are nearly always spindle shaped or round, lying in a fine connective-tissue stroma. The spindle-cells vary greatly in size and in

the amount of pigment. This is distributed in the usual manner (*see* "Sarcoma of the Choroid"). Eleven cases of leuco-sarcomata have been recorded, but parts of melanotic sarcomata are often unpigmented.

Pure round-celled sarcomata and those with mixed round- and spindle-cells are uncommon; the former are liable to be mistaken histologically for inflammatory conditions, and *vice versâ*. Karyokinetic figures and cells with two or more nuclei are almost invariably absent, a striking difference from any other sarcomata. It is probably evidence of the slow rate of growth, which is further emphasised by a sort of pseudo-alveolation. No trace of degenerative changes or inflammatory reaction is usually found. Coleman's case (*see* Wood and Pusey) of "round-celled, pigmented sarcoma" with marked œdema and infiltration with polymorphonuclear leucocytes was probably purely inflammatory.



FIG. 230.—SARCOMA OF IRIS. × 60.

The growth is chiefly spindle celled, with very little pigment. It has some resemblance to Fig. 229, but the nuclei are more oval than rod shaped.

The growth generally starts in the anterior layers of the iris, but occasionally in the posterior layers (Kerschbaumer). A pseudo-alveolar structure is often very marked; the cells are frequently arranged in rows and whorls, with little intercellular substance. These cells are probably derived from the adventitia of the vessels, and many of these growths are peritheliomata. Most of the pigmented spindle-cells are undoubtedly derived from the stroma-cells of the iris. In at least eleven cases, and with great probability in several others, the tumours have grown from congenital nævi (Treacher Collins, Ewetzky, Hirschberg, Hosch, Whiting). Most of these are probably melanomata of Fuchs's first type (*v.* p. 324) which have taken on malignant proliferation. Whether any are melano-carcinomata derived from true nævi must be left a matter of doubt until further evidence is available. The presence in the tumour of pigmented epithelial cells

derived from the pars iridica retinæ must be ignored in this connection; they are of the same nature as those found by Leber[1] in sarcoma of the choroid, derived from the hexagonal pigment-cells.

Leuco-sarcomata of the iris have been described by Alt, Treacher Collins, Marshall, Thalberg, Limbourg, and others. Limbourg's case showed the clinical picture of "serous iritis" with keratitis punctata; the deposits upon the back of the cornea may have been sarcoma-cells (v. Michel).

Secondary sarcoma of the iris is more common than primary (Fig. 263, p. 368). It usually arises by continuity, but may also be metastatic, and is then probably invariably *viâ* the lymph-stream and not the blood. Multiple local metastases in the iris are not very uncommon in sarcoma of the ciliary body (Ginsberg). Secondary sarcoma by continuity often infiltrates the iris diffusely without forming any definite tumour, as in a case which I have reported (Fig. 267).

TAY.—R. L. O. H. Rep., v, 1866. KNAPP.—A. of O., viii, 1879. FUCHS.—Das Sarcom des Uvealtractus, Wien., 1882. TREACHER COLLINS.—R. L. O. H. Rep., xii, 1889. EWETZKY.—A. f. O., xlii, 1, 1896; xlv, 3, 1898. WERTHER.—A. f. A., xxxii, 1896. *CASEY WOOD AND BROWN PUSEY.—A. of O., xxxi, 1902. MARTIN.—Inaug. Diss., Halle, 1885. LAWFORD AND TREACHER COLLINS.—R. L. O. H. Rep., xiii, 1893. BRUDENELL CARTER.—Med. Times and Gazette, 1874. KERSCHBAUMER.—Das Sarcom des Auges, Wiesbaden, 1900. HIRSCHBERG.—A. f. O., xiv, 3, 1868. HOSCH.—C. f. A., v, 1881. WHITING.—A. of O., xix, 1890. ALT.—Amer. Jl. of O., 1887. MARSHALL.—T. O. S., xvii, 1897. THALBERG.—A. of O., xiii, 1884. LIMBOURG.—A. of O., xix, 1890. PARSONS.—A. f. O., lv, 2, 1903; A. of O., xxxiii, 1904. *LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. KAYSER.—K. M. f. A., xli, Beilageheft, 1903.

CARCINOMA

The only epithelial structure in the iris is the pars retinalis iridis; hence, according to the received nomenclature, *primary* carcinoma of the iris could only originate in this layer. I have already considered melanomata, which are benign tumours springing from the stroma or from the retinal epithelium. When these become malignant they assume the characters of sarcomata, and probably always belong to the first class; whether the epithelial melanomata become malignant must be left open to doubt, just as it is doubtful whether true nævi of the dermal type occur or cause malignant neoplasms in the iris.

Extremely few records of primary carcinoma of the iris are found in the literature, and the cases are all open to other and, on the whole, more probable interpretation. W. Robertson described a carcinoma involving the iris and ciliary body originating in the pigment epithelium. Epithelioid cells, showing extensive colloid degeneration, were gathered together in groups surrounded by fibrous tissue, thus giving the picture of a scirrhous cancer. The diagnosis is upheld by Lagrange, but most authors would prefer to regard the growth as an endothelioma or alveolar sarcoma (Emmanuel).

Hirschberg and Birnbacher described a "spongy cancer of the posterior layer of the iris." It occurred in a man of twenty-six, and was

[1] LEBER.—A. f. O., xliv, 3.

preceded by inflammatory symptoms. There was a spongy grey mass on the back of the iris which displaced the lens backwards. It consisted of large epithelial cells, with normal or vacuolated nuclei, arranged in cords or tubes without any intercellular stroma. The tubes were formed from the cords by hydropic degeneration of the central cells. Between them, especially in the posterior part, was non-nucleated fibrous tissue, containing wide blood-channels, which did not even possess endothelial walls. The fibrous tissue was considered to be degenerated vitreous. Many of the cells contained pigment granules. The iris showed chronic inflammatory changes, with partial separation of the two layers of pigment epithelium, and nodules of epithelial pigment-cells similar to those of the tumour. The ciliary body was compressed, but not involved in the growth.

The nature of this neoplasm is doubtful. Emmanuel[1] regards it as inflammatory; Lagrange, again, supports the author's diagnosis. Ginsberg points out that it differs from carcinoma in growing only from the surface without invading other tissues and in possessing no stroma; and from atypical epithelial proliferation of inflammatory origin in bursting the fibres of the zonule and in forming isolated nodules on the surface of the iris; moreover, the ciliary body showed no trace of inflammation. In spite of these criticisms, the inflammatory theory seems the more probable. There was history of inflammatory attacks, and the tension is said to have been +2, neither of which statements are consistent with absence of signs of inflammation in the ciliary body. There is also a note of red corpuscles, mononuclear and, in smaller numbers, polynuclear leucocytes in the fibrous tissue about the growth. Further, the structure is not inconsistent with inflammatory hyperplasia such as is seen more frequently in the ciliary body (q. v.), especially when combined with œdema.

There are several cases on record of *secondary* carcinoma of the iris by continuity from metastatic growth in the choroid; at the same time the iris is seldom implicated in these cases. In Ewing's case the iris was largely transformed into fibrous tissue, amongst which lay plugs of cancer-cells; there were also nodules on the anterior surface, below which the vessels were blocked with cancerous thrombi. These were found in the posterior ciliary arteries by Abelsdorff, but not in the iris vessels. This author and v. Michel consider that the iris is involved by dissemination, not by continuity or embolism. There does not seem to be much in favour of this view, though in Lagrange's case, as also in Abelsdorff's, the iridic tumour was not in direct continuity with the main growth.

W. Robertson.—Ophth. Rev., xiv, 1895. Hirschberg and Birnbacher.—C. f. A., xx, 1896. Ewing.—A. f. O., xxxvi, 1890. Abelsdorff.—A. f. A., xxxiii, 1896. Lagrange.—Tumeurs de l'Œil, i, Paris, 1901.

[1] Emmanuel.—Virchow's Archiv, clxi, 1900.

TUMOURS OF THE ANGLE OF THE ANTERIOR CHAMBER

ENDOTHELIOMA

Endothelioma is the only *primary* growth of the angle of the

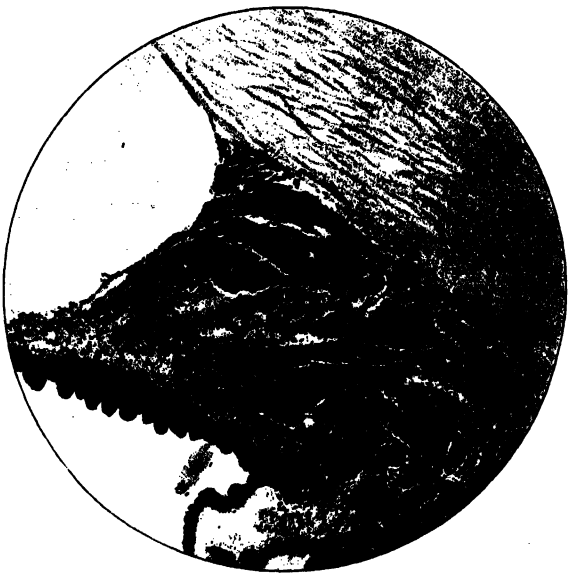


FIG. 231.—ENDOTHELIOMA OF LIGAMENTUM PECTINATUM IRIDIS. × 55.
From a specimen sent by Prof. Fuchs. This is doubtless the case described and figured by Hanke in A. f. O., xlvii.

anterior chamber, if we except tubercle. A unique case has been described by Hanke from Fuchs's clinic (Fig. 231). It consisted partly



FIG. 232.—GLIOMA RETINÆ IN ANGLE OF ANTERIOR CHAMBER. × 55.
From a girl æt 6. Appearance of flocculent hypopyon in lower angle. There was extensive glioma endophytum. The figure shows the lower false angle covered with glioma-cells. The nodule on Descemet's membrane, resembling k. p., shows central well-stained cells and peripheral necrotic cells.

of polygonal endothelial cells derived from the ligamentum pectinatum iridis and partly of spindle- and star-shaped pigmented cells and round

cells. All the cells were pigmented, the polygonal least and the round cells most; there were also clumps of free pigment granules between the cells and in the vessels. The cells were arranged in an alveolar manner. The growth had invaded the cornea, iris, and ciliary body, and the perivascular lymph-channels were pervaded with tumour-cells. Hanke considers that the endothelium is normally pigmented in this

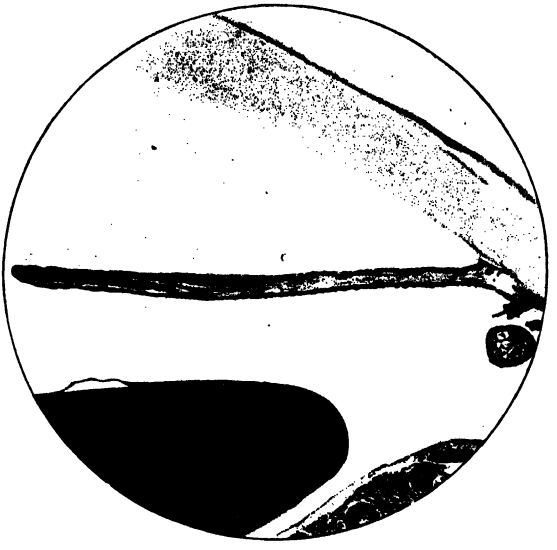


FIG. 233.—GLIOMA RETINÆ COVERING IRIS. × 17.

Narrow peripheral anterior synechia; retro-lental part of globe full of glioma. The iris is covered by a thin layer of glioma-cells lying upon minute capillaries, thus giving an arcade-like appearance. Note masses of glioma near ciliary processes and behind lens.

situation, basing his observation on Rochon-Duvigneaud's researches, though, as Ginsberg points out, this author speaks only of a pigmented connective-tissue framework.

HANKE.—A. f. O., xlvii, 3, 1899.

SECONDARY GROWTHS

Infective **granulomata**—tubercle, gumma, etc.—of the iris or ciliary body often invade the angle of the anterior chamber.

So, too, **sarcoma** of the ciliary body frequently invades the angle, producing the clinical appearance of an irido-dialysis (*see* "Ciliary Body"). There is a great tendency in some cases for the infiltration to extend around the whole circle of the angle, thus forming an *annular* or *ring sarcoma* (Meyerhof, Kopetzky v. Rechtperg, Parsons).

MEYERHOF.—K. M. f. A., xxxix, 1901. KOPETZKY V. RECHTPERG.—A. f. O., lii, 2, 1901. PARSONS.—A. f. O., lv, 2, 1903; A. of O., xxxiii, 1904.

Glioma.—Secondary deposits are often found in the angle of the anterior chamber (Fig. 232) and on the surface of the iris in cases of

glioma retinæ. They are caused by dissemination of the cells by the lymph-streams, which is so marked a feature of this neoplasm. I have seen the iris covered by a thin layer of glioma-cells, which did not invade the structure itself (Fig. 233); the whole iris, indeed, may be embedded in the growth and yet unaffected (Wintersteiner). Actual invasion is a very late phenomenon. Wintersteiner also found miliary nodules under the pigment epithelium, which was partly atrophic and partly hyperplastic.

These superficial nodules, in common with those on the choroid, Descemet's membrane, etc., are non-vascular, and therefore often partially or totally necrotic (*see* "Glioma Retinæ").

WINTERSTEINER.—Das Neuroëpithelioma Retinæ, Wien, 1897.

CHAPTER VI

THE CILIARY BODY

THE NORMAL CILIARY BODY

THE ciliary body consists of two parts, the anterior folded part, *corona ciliaris*, carrying the seventy to eighty ciliary processes, and the posterior smooth part, *orbiculus ciliaris*. In meridional section it resembles an isosceles triangle with the apex backwards; here it is continuous with the choroid. From near the middle of the base the iris springs.

The ciliary body is composed chiefly of the ciliary muscle, together with vessels and nerves bound together by connective tissue. The vessels are numerous, the ciliary processes consisting almost entirely of them, reminding one of the renal glomeruli. Most of the vessels lie between the ciliary muscle and the pars ciliaris retinæ. The connective tissue is fibrillar, becoming coarser and more hyaline in old age, and contains numerous branched cells, many of which are pigmented. There are many elastic fibres throughout, but they are gathered together at the outer part of the base into circular and oblique bundles, which form a ring and are continuous with those of the ligamentum pectinatum iridis. On the inner side, the elastic fibres join an elastic lamina, which lies between the ciliary muscle and the chief bundles of vessels, passing backwards to join the lamina vitrea of the choroid. The latter splits anteriorly into two layers, an outer, the elastic lamina already mentioned, and an inner, hyaline non-elastic membrane, which lies immediately beneath the retinal epithelium, and is called by Salzmann the *outer hyaline membrane* (Glashaut) of the ciliary body. This is to distinguish it from an *inner hyaline membrane* which this author describes lying upon the retinal epithelium, continuous posteriorly with the hyaloid membrane of the vitreous body. The fibres of the *zonule of Zinn* arise from this inner hyaline membrane (Salzmann). There is a network of elastic fibres among the vessels between the elastic lamina and the outer hyaline membrane.

The ciliary muscle (Bowman) consists of two parts, the outer meridional, *Brücke's muscle*, and the inner circular, *Müller's muscle*. Both are made up of unstriped fibres, and are variously developed in different eyes, the former most in myopic, and the latter in hypermetropic eyes. The difference in development is present in the newborn (Lange). Brücke's muscle arises from the sclerotic internal and

posterior to Schlemm's canal, and is gradually lost posteriorly in the external layers of the choroid; hence the term tensor choroideæ (Brücke). Waldeyer describes a small outer portion inserted into the



FIG. 234.—GLANDS OF THE CILIARY BODY. × 120.
From Treacher Collins. Bleached section of normal human ciliary body.

sclerotic, homologous with the *Crampton's muscle* of birds. The ciliary muscle consists of striped fibres in birds.

The *pars ciliaris retinæ*, covering the inner surface of the ciliary body, consists of two layers of the epithelium, corresponding with the two layers of the secondary optic vesicle. The outer layer is pigmented, the cells being higher than those covering the choroid, except at the tips of the ciliary processes. The inner layer is non-pigmented, the cells being

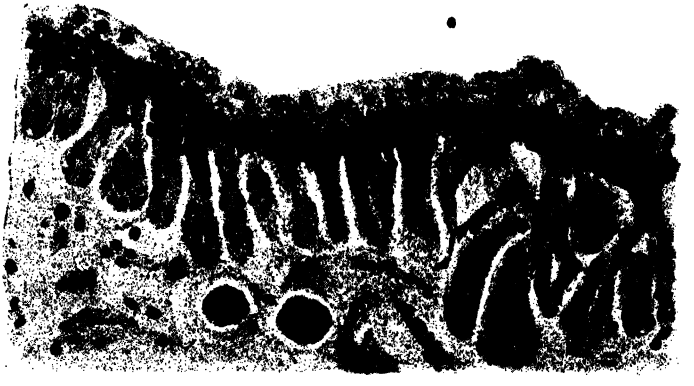


FIG. 235.—GLANDS OF CILIARY BODY. × 300.
From Treacher Collins. Bleached section of normal eye.

cubical or cylindrical. The epithelium lies upon the outer hyaline membrane, which has irregular thickenings upon its inner surface, forming a sort of reticulum, which has large meshes in the posterior part of the orbi-

culus and smaller meshes near the corona. The reticulum is best seen at about fourteen years of age (Kuhnt, Salzmann). The meshes are filled in with pigment epithelium, and when this is bleached the depressions resemble glands. These are the *glands of the ciliary body* (Treacher Collins) (Figs. 234, 235); they pass down towards the elastic lamina, seldom below it.

KUHNT.—K. M. f. A., xix, 1881. TREACHER COLLINS.—T. O. S., xi, 1891; Ophth. Rev., xv, 1896; Researches, London, 1896; *see also* NICATI, A. d'O., x, 1890; xi, 1891; BUCHANAN, Jl. of Anat. and Phys., xxxi. GRIFFITH.—Ophth. Rev., xiii, 1894. ALT.—Am. Jl. of Ophth., xiii, 1896. SALZMANN.—Die Zonula ciliaris u. ihr Verhältniss zur Umgebung, 1900. LANGE.—K. M. f. A., xxxix, 1901.

WOUNDS

Wounds of the ciliary body are of peculiar interest to the clinician, and have received much attention from the clinical standpoint on account of their liability to set up sympathetic ophthalmia. They are often associated with prolapse of the iris and ciliary processes, resulting in iritis and cyclitis. The microscopical changes accompanying traumatic cyclitis are described elsewhere (*v. infra*). It often goes on to suppuration and the loss of the eye. In cases where infection is avoided the wounds heal rapidly, as might be expected in so vascular a tissue. The process of healing resembles that of the choroid, which will be treated fully in considering wounds of the retina. The pars ciliaris retinæ takes no part in the process at all, except that the pigment-cells of this layer sometimes show proliferation, but only in slight degree. The sclerotic, too, is absolutely inert, the edges being clean cut though slightly rounded off, and the new cells running almost entirely at right angles to them (Fig. 236). The ciliary body provides fibroblasts for a modicum of the scar tissue; others are derived from the episcleral tissue. Some proliferation of the pigment-cells occurs; pigment is found in small quantities scattered through the scar, mostly as free granules, some in leucocytes, and some—the smallest part—in pigment-cells, most of which are of uveal origin, though some appear to be retinal.

PARSONS.—R. L. O. H. Rep., xv, 3, 1903.

INFLAMMATION

ACUTE AND SUPPURATIVE

Acute and suppurative cyclitis are seen after perforating wounds of the globe, corneal ulcers, in panophthalmitis, etc.; there is no sharp limit anatomically between the two conditions.

The first sign of acute cyclitis is intense hyperæmia, with dilatation of the vessels, which are packed with red corpuscles and surrounded by leucocytes, these being also more numerous inside the vessels. The connective tissue is most affected, the ciliary muscle escaping to a large extent. The former is œdematous and densely crowded with mono- and

polymorphonuclear leucocytes, which obscure the normal structures. The mast-cells, which are normally present in small numbers, are much multiplied. Even in very early stages, *e. g.* during the first hours after an injury, the leucocytes are not confined to the ciliary body itself, but penetrate between the retinal epithelial cells and escape into the vitreous, the posterior chamber, etc. (Figs. 237, *sqq.*), and are carried by the lymph-stream into the anterior chamber, where they may accumulate and form an hypopyon. The iris is invariably inflamed in greater or less degree. The lymph secreted by the inflamed ciliary processes contains an excess of proteids, and is readily coagulable. The coagulum varies greatly in the amount of fibrin present. This may be almost absent, so that the hypopyon is fluid; in this case the cells may break



FIG. 236.—WOUND OF THE CILIARY BODY. × 25.

Parsons, R. L. O. H. Rep., xv, 3. Perforating wound of ciliary body of a monkey, made with a Graefe knife fourteen days previously; equatorial section.

up and pass away through the normal channels of excretion at the angle of the anterior chamber, though they are frequently reinforced and a fresh hypopyon forms. In the more acute and more plastic forms of inflammation the exudate in the vitreous, amongst the fibres of the zonule, in the posterior chamber, pupillary area, and anterior chamber, may be composed of a dense network of fibrin containing leucocytes in its meshes (Fig. 244). The more solid hypopyon present under these conditions is less readily disposed of, and may subsequently organise. Still more resistant are the coagula behind the iris, and it is around the lens in this situation that the first traces of fibrous organisation appear, even as early as the eighth day (Buchanan) (Fig. 243).

It can scarcely be doubted that the infiltrating cells are entirely of hæmal or lymphatic origin; the development of leucocytes from endo-



FIG. 237.—CYCLITIS. × 9.

Buchanan, T. O. S., xxi. Cyclitis of fourteen days' duration. Exudate in the vitreous, lying upon the ciliary body, retina and lens capsule.



FIG. 238.—CYCLITIS. × 14.

Buchanan, T. O. S., xxi. Cyclitis of many years' duration. Corneo-scleral junction above to right; lens above to left. Below the lens is a mass of fibrous tissue with the ciliary body to the right, and the detached and folded retina below.



FIG. 239.—CYCLITIS. × 100.

Buchanan, T. O. S., xxi. Cyclitis of twenty days' duration. Section of pars ciliaris retinæ, showing the process of deposition of the exudate.



FIG. 240.—CYCLITIS. × 100.

Buchanan, T .O. S., xxi. Cyclitis of sixteen days' duration. Section bleached with euchlorine.



FIG. 241.—CYCLITIS. × 120.

Buchanan, T. O. S., xxi. Cyclitis of twenty-two days' duration. Showing the inner surface of the retina and separation of the vitreous, with large epithelioid cells lying in the intervening space.

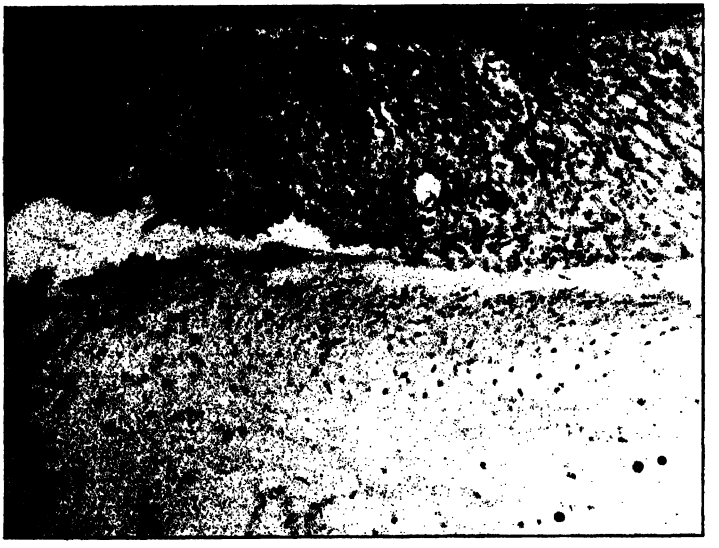


FIG. 242.—CYCLITIS. × 120.

Buchanan, T. O. S., xxi. Cyclitis of twenty-two days' duration. Showing the inner surface of the retina and the vitreous.



FIG. 243.—CYCLITIS. × 200.

Buchanan, T. O. S., xxi. Cyclitis of sixty days' duration. Pars ciliaris retinæ above. Showing the formation of fibrous tissue in the exudate.

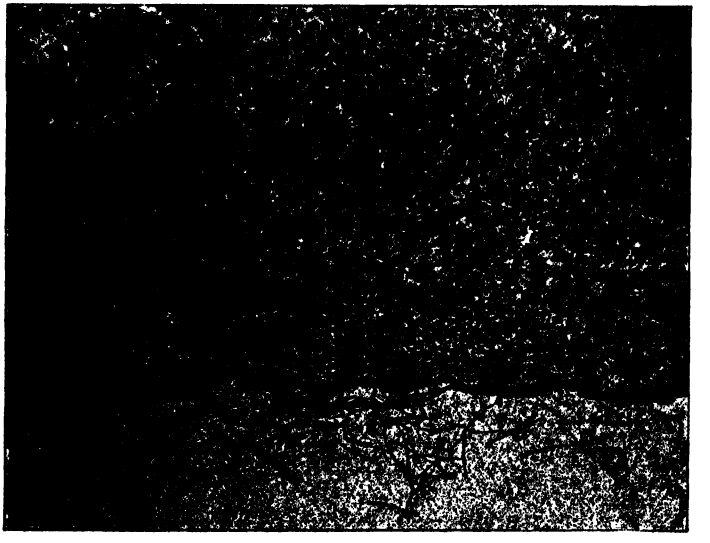


FIG. 244.—CYCLITIS. × 100.

Buchanan, T. O. S., xxi. Cyclitis of eighteen days' duration. Showing fibrinous exudate below.

thelium and fixed tissue-cells (Reid, Buchanan) is opposed to the opinions of the best pathologists. In suppurative cyclitis the polymorphonuclear leucocytes are greatly in excess, and are densely aggregated upon the surface of the ciliary body (Fig. 193, p. 293).

The two layers of epithelium upon the ciliary processes are often separated by exudate, and this occurs more frequently than in the iris. Both layers of epithelium may also be raised from the rest of the ciliary body by exudate. In this manner quite large cystic spaces may be formed; they have been found after puncture of the anterior chamber in rabbits (Greeff) (*v. infra*).

Desquamation of the epithelium is found, and this especially affects the pigmented layer. The cells break up and set free their pigment granules, which are disseminated amongst the cells and are largely taken up by leucocytes. It is not uncommon to find the ciliary processes almost entirely deprived of their pigment, especially in cases of panophthalmitis, and the glands of the ciliary body may often be well demonstrated.

In the more severe cases the inflammation is not confined to the anterior part of the eye, but a condition of panophthalmitis is set up. The retina then becomes inflamed; its vessels are dilated and surrounded by leucocytes, which may later add their quotum to the exudate in the vitreous.

Organisation of the exudate resembles cicatrisation in other parts of the body. Fibroblasts are formed from the fixed connective-tissue cells, and invade the exudate, manifesting themselves as large spindle- or star-shaped cells (Fig. 243). There is no good evidence that the cubical cells of the retinal epithelium contribute to the formation of fibrous tissue, as stated by Alt. They are often dragged out and appear cylindrical. New blood-vessels are formed in the usual manner, solid processes being given off from the capillary walls. These become canalised, and appear as simple endothelial tubes, which later assume an adventitial connective-tissue sheath. The fibrous tissue increases rapidly, being loose and cellular at first, with fine wavy fibrils and often large hyaline masses, especially in the vitreous. In the later stages, and in some cases relatively early, dense masses of closely packed fibres with few cells or blood-vessels are laid down. This, in typical cases, forms a thick membrane behind the lens, being attached to the ciliary body on each side, and frequently sending off processes which are attached to the retina. During the contraction which always accompanies the consolidation of such tissue the ciliary processes are drawn inwards, and the whole ciliary body is often detached from the sclerotic, except at the spot where the ciliary muscle is inserted into the sclerotic just behind the angle, leaving a large supra-ciliary space, traversed by fine, more or less concentric laminæ of pigmented stroma. The retina is also detached by the same process, the globe finally shrinking and entering into the condition known as *phthisis bulbi*.

A less common metamorphosis of the exudate is seen in the formation of lamellæ of homogeneous material, separated by flattened, branched cells.

In all types there is frequently marked proliferation of the pars ciliaris retinæ into the scar tissue. Long, branching, pigmented bands

are thus formed (Alt); these, on bleaching, are seen to consist of tubules lined with cylindrical or flattened epithelium (Figs. 245—7). They arise chiefly from the pars plana, and give the appearance of proliferation of the glands of the ciliary body (Treacher Collins) (Fig. 245). Blood-corpuscles may occasionally be seen inside similar pigmented tubules lined with flattened cells, so that these tubes are probably new-formed blood-vessels, the pigment around them being hæmatogenous. In some cases plugs or tubes of non-pigmented epithelium are seen in the same situation, derived from the retinal epithelium. There is some evidence that these may later become pigmented (Treacher Collins).



FIG. 245.—TUBULES IN CYCLITIC MEMBRANE. × 300.
From Treacher Collins.

The lens is often completely embedded in dense fibrous tissue, which occludes the pupil, leads to total posterior synechia and the formation of a cyclitic membrane in the vitreous. The lens capsule remains intact, though it is often wavy and folded owing to the degenerative changes which take place in the lens and lead to shrinking. The lens under such circumstances may become calcareous, but never bony, as long as the capsule is intact; this apparently forms a barrier impassable to osteoblasts.

The various stages of exudation and organisation may often be seen simultaneously in different parts of the same section. The part nearest the ciliary body naturally organises first, since it is from this part that the fibroblasts are derived. Here the fibrous tissue lies upon the broken up and distorted retinal epithelium, between the cells of which



FIG. 246.—TUBULES IN CYCLITIS. × 55.

Contusion twenty years before excision. On the right, sclerotic. To the left of this non-pigmented tubules are seen growing from the pars plana into a mass of post-cyclitic fibrous tissue. The fibrous tissue to the left is more cellular, and has undergone fatty degeneration.

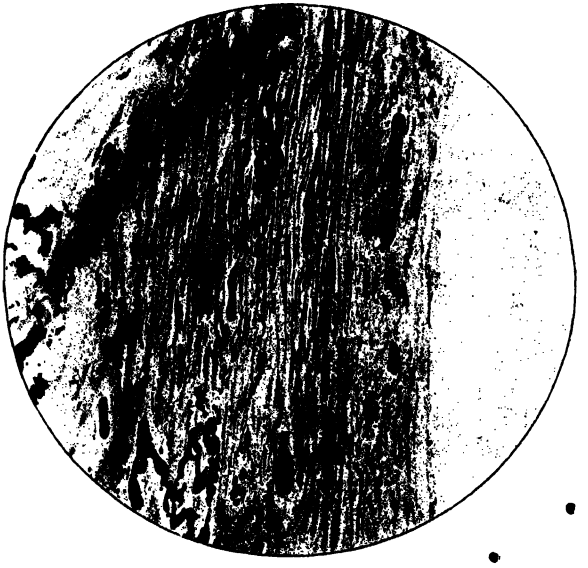


FIG. 247.—TUBULES IN CYCLITIS. × 60.

Cyclitis of thirty-five years' duration. The sclerotic is to the left beyond the field. Pigmented tubules in dense post-cyclitic fibrous tissue. The amount of pigment varies, and is absent from some of the tubules.



FIG. 248.—CYCLITIS. × 100.

Buchanan, T. O. S., xxi. Cyclitis of two and a half months' duration. Showing fatty degeneration of the exudate.

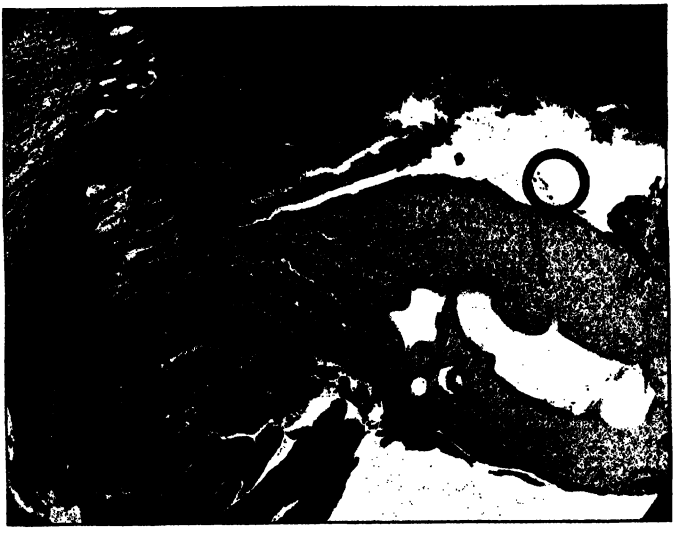


FIG. 249.—CYCLITIS. × 15.

Buchanan, T. O. S., xxi. Cyclitis after seventeen years. Showing true bone in the curve of the displaced ciliary body.

blood-vessels pass. Internal to the fibrous tissue is a fibrinous cellular exudate (Fig. 243).

Buchanan describes five types of cell in the exudate, and explains their origin as follows:—(1) A multinuclear cell with finely granular protoplasm actively engaged in proliferation; a leucocyte or dividing mononuclear cell; (2) a mononuclear cell, which proliferates: a lymphocyte (*a*) of vascular origin, (*b*) a bud from other exudation-cells, (*c*) a bud from fixed cells; (3) a large epithelioid cell, occasionally dividing: a retinal epithelial cell; (4) a small round mass of nuclear matter, probably a young cell: a bud; (5) a large mass of more or less ill-defined protoplasm without nucleus, or "ghost-cell:" the cytoplasm from which a nucleus has passed out. He considers that nuclear activity is displayed by (*a*) gemmation, or budding, (*b*) fission, (*c*) fragmentation, (*d*) emigration; karyokinesis is not seen, being too slow a method of cell-division. Buchanan's observations and preparations are of great value, but his deductions are not wholly in accord with generally accepted views.

Degenerative changes occur in the exudate and cicatricial tissue. The earliest of these, apart from fragmentation of nuclei, which is a sign of necrosis, is fatty degeneration (Buchanan) (Fig. 248). Lime-salts are frequently deposited in the membranes and fibrous masses, first as fine granules or concretions which stain very deeply with hæmatoxylin and other dyes containing alum (Figs. 250, 251). At a later stage true bone may be formed (Figs. 249—253).

Bone formation in scars is of extreme rarity in other parts of the body. It frequently occurs in degenerative, usually post-cyclitic, conditions in the choroid. It would seem as if the choroid and in less degree the ciliary body possess the capacity of forming osteoblasts from their fixed cells instead of fibroblasts under definite conditions of prolonged irritation and degeneration. The formation of bone in cyclitic deposits is comparatively rare. It commences in the deposition of spherical globules, usually in proximity to a blood-vesse The granules coalesce and form a homogeneous mass, which may be shown to contain calcium carbonate (Fig. 251). The edges are ragged and terminate in globules, which diminish in size as they are farther from the mass.

At an early stage long delicate fibres, and occasionally stellate corpuscles may be seen lying between the globules and radiating from the mass into the surrounding tissue (Fig. 253). These are evidently comparable with osteogenetic fibres and osteoblasts (Buchanan). The more advanced portion of the mass early encloses the blood-vessel, and soon shows a marked change in structure; it becomes striated concentrically around the irregular cavity in which the blood-vessel lies (Fig. 252).

At a later stage the spaces are seen to be lined with osteoblasts regularly arranged, and to contain, besides the blood-vessel, fat and sheaves of fatty crystals. In the completely formed bone the cavities are more open and the lamination is more marked. The growing edge of the bone continues to be ill defined, and consists usually of a series of fibres, which pass outwards into the surrounding fibrous tissue. The



FIG. 250.—CYCLITIS. × 15.

Buchanan, T. O. S., xxi. Cyclitis after eleven years. Showing an early stage in the formation of bone in the exudate. The upper, less advanced part is opaque and granular; the lower, more advanced part bears some resemblance to bone.

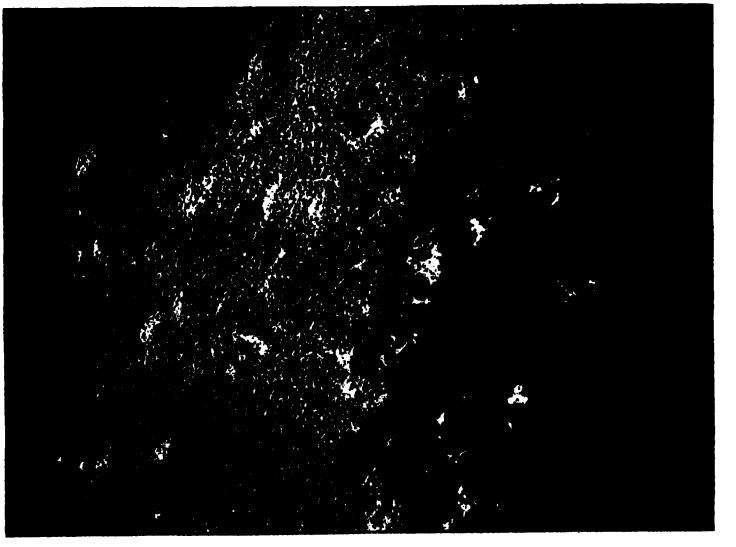


FIG. 251.—CYCLITIS.

Buchanan, T. O. S., xxi. Cyclitis after eleven years. Showing the deposition of calcareous particles.



FIG. 252.—CYCLITIS. × 150.

Buchanan, T. O. S., xxi. Cyclitis after thirteen years. Showing the structure of fully formed bone. A cavity lined with osteoblasts is seen.



FIG. 253.—CYCLITIS. × 150.

Buchanan, T. O. S., xxi. Cyclitis after twenty years. Showing the connections of advancing bone formation. Fibres are spread out, with cells between them.

cells arrange themselves in columns around these fibres, and both appear to be surrounded by calcareous deposit.

ALT.—Lectures on the Human Eye, New York, 1880. TREACHER COLLINS.—Researches into the Anatomy and Pathology of the Eye, London, 1896. *BUCHANAN.—T. O. S., xxi, 1901.

CHRONIC CYCLITIS

Chronic cyclitis, or irido-cyclitis, occurs in two forms: (1) *serous cyclitis*, often called "serous iritis"; (2) *chronic plastic cyclitis*, which is merely a subacute or chronic plastic cyclitis, similar in its essentials with the non-suppurative forms of acute cyclitis.

The characteristic physical sign of *serous cyclitis* is the presence of deposits upon the back of the cornea, commonly known by the ill-chosen term, *keratitis punctata* (Sichel). These precipitates appear as minute greyish dots scattered irregularly upon Descemet's membrane, but mostly over a triangular area of the lower part; the base of the triangle corresponds with the lower corneal margin, the apex being directed upwards towards the centre of the cornea. The larger deposits are usually below, the more numerous finer ones above, but the typical arrangement is often wanting. The spots are frequently pigmented, looking brown or reddish. Larger aggregations occur in older cases, and the deposits then often assume a yellowish gelatinous appearance, sometimes known in England as "mutton-fat k. p."

These deposits have long been recognised. They were first accurately described by Wardrop (1808), and attributed by him to inflammation of Descemet's membrane—Descemetitis, hydromeningitis, aquocapsulitis, keratitis punctata. Ruete (1845) and Stellwag v. Carion first pointed out that inflammation of a structureless membrane like Descemet's cannot occur, and further that this membrane does not extend over the iris and has nothing to do with the secretion of aqueous. Arlt (1853) regarded the deposits as a product of iritis, and v. Graefe (1856) showed ophthalmoscopically the frequent participation of the choroid in the inflammation in these cases.

Schweigger (1873) and Iwanoff (1876) give the first description of the microscopic appearances, which they considered due to the proliferation of the endothelium of Descemet's membrane.

de Wecker (1876) describes a fibrinous exudate as occurring first at the spots, followed later by proliferation of the endothelial cells. Knies (1880) found small groups of round-cells, under which the endothelium was intact and unchanged; in later stages, and in the case of larger deposits, the endothelium had disappeared, and the round-cells showed degenerative changes, their contours being indistinct. He observed similar exudates upon the surface of the ciliary body, but doubted their ability to traverse the zonule of Zinn. He therefore attributed those on the back of the cornea to iritis; we now know that such exudates can be readily carried forwards by the lymph-stream, passing between the fibres of the zonule, which does not form an impenetrable membrane. Fuchs (1884) first brought forward incontrovertible anatomical evidence that the

deposits are a sign of chronic cyclitis, and that they are chiefly derived from the ciliary body. He found them to consist of aggregations of leucocytes (Fig. 254), many of which contained pigment granules, showing their origin from the uveal tract. The cells usually have large nuclei and a small amount of cytoplasm, so arranged as to resemble a signet-ring. The precipitates lie upon the endothelium of Descemet's membrane, which is at first quite normal; later, and under larger deposits, the endothelium degenerates and disappears. The endothelium is therefore not in most cases the active cause of the deposits. In late stages the cells undergo fatty degeneration and become absorbed, leaving the pigment granules behind. These then appear as fine pigmented spots. Schweigger (1885) described proliferation of the endothelium around the deposits; he considered them to consist of detritus

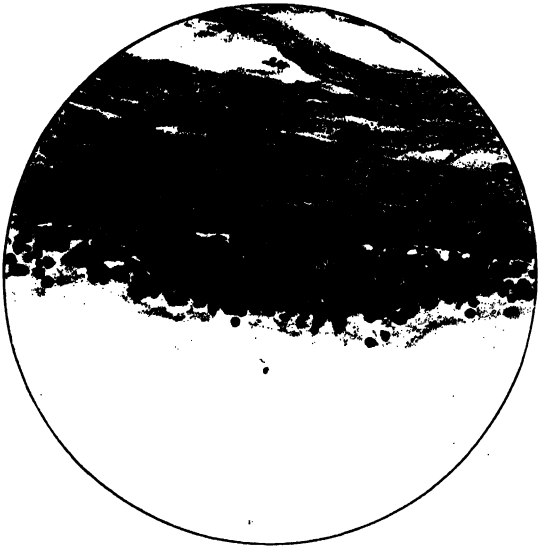


FIG. 254.—"KERATITIS PUNCTATA." × 200.

"Mutton-fat k. p." from case of irido-cyclitis. The figure shows a mass of leucocytes on Descemet's membrane, the endothelium of which is intact. The centre of the mass consists of fibrin and granular material, the periphery of fibrin. There were many such nodules in the lower part of the a. c.

and degenerated cells deposited on the back of the cornea, and easily washed off, *e.g.* by the escape of aqueous on puncturing the anterior chamber. Snellen, Jr. (1894) found groups of bacteria in the deposits; this observation has not been confirmed for ordinary keratitis punctata, and must be of rare occurrence. Ridley (1895) confirms the results of earlier observers, including the normal condition of the endothelium in the early stages. That proliferation of the endothelium may, however, occur has been shown by Uhthoff and Axenfeld (1896). They obtained warty endothelial growths after inoculation of pneumococci into the anterior chamber of rabbits. Grœnouw (1900) found pigment granules partly within and partly outside the cells; he also

found giant-cells, or bodies resembling them, and a network of fibrin between the cells and often lying upon the intact endothelium, which he thinks plays a purely passive part.

Whilst the leucocytes which form these precipitates are commonly derived mainly from the ciliary body, Baas (1903) has adduced good evidence that they may come from the iris alone. In his case there was total posterior synechia, and a fresh attack of inflammation was followed by new deposits; these could not have passed through the iris, but must have been derived from it.

The pigment was derived by Leber (1879) from degenerated red corpuscles; in the majority of cases it is undoubtedly uveal (Knies, Fuchs, Groenouw). Probably it may originate from either source.



FIG. 255.—"KERATITIS PUNCTATA." × 55.

From a case of dislocated lens. The figure shows the lower part of the ciliary body, covered with swollen leucocytes, undergoing hyaline degeneration. Large nodules of the same cells were present over the lower part of Descemet's membrane. Note the degeneration of the iris and ciliary body. The section was stained by van Gieson, and shows the dense bands of fibrous tissue in these structures.

The larger deposits of long standing, which are known clinically as "mutton-fat k. p.," show a hyaline degeneration of the cells (Fig. 255). These are swollen, and run together more or less; the nuclei stain badly or not at all, though their outlines can often be made out dimly. The masses stain with cytoplasmic stains, but diffusely with nuclear stains.

There can be little doubt that the cells are deposited centrifugally upon the back of the cornea, and that the movements of the eyes are a factor in determining their arrangement (Arlt). The spots are occasionally seen upon the lens capsule; it would be impossible for them to be derived here from endothelium, but the absence of

endothelium may account for the infrequency of their occurrence in this situation. It is probable that in the conditions under which they occur the endothelium of Descemet's membrane is irritated and becomes sticky, so that the leucocytes readily adhere to it.

Deposits resembling keratitis punctata may arise from other causes, usually malignant growths. v. Michel describes a round-celled sarcoma of the ciliary body in which nodules of tumour-cells were found upon the back of the cornea, the endothelium being normal. Similar deposits of glioma-cells may occur (*v.* p. 333).

Whilst the aqueous in serous cyclitis is richer in proteids than the normal fluid, yet there is less tendency to coagulation than in acute cyclitis. The inflammation is more of the catarrhal than the plastic



FIG. 256.—CYCLITIS, SHOWING RETRACTION OF THE IRIS AT THE PERIPHERY. × 25.

Cornea in front to left; peripheral anterior synechia, retraction of periphery of iris. The iris is degenerated; note the new fibrous membrane on anterior surface, most marked near pupillary edge, to right; also "ectropion of uvea." The ciliary processes are dragged inwards and lie in a mass of almost non-cellular fibrous tissue, which fills the posterior chamber and replaces the vitreous. The material to the right below is coagulum behind the detached atrophic retina.

type, and the exudate is relatively poor in fibrin. Such considerations have led Treacher Collins to regard the condition as a catarrh of the glands of the ciliary body.

The anatomical changes which occur in the ciliary body differ chiefly in degree from those found in acute cyclitis. The ciliary processes are moderately swollen, and may touch the back of the iris (Fuchs). The tissues are infiltrated with leucocytes, which are chiefly arranged around the blood-vessels, but may also occur in nodular masses, especially in the posterior part of the ciliary body. These consist mostly of mononuclear lymphocytes, and are found especially

between the ciliary muscle and the pigment epithelium. The latter may be little altered, the exuded cells passing between the epithelial cells into the vitreous. Here they form masses on the inner surface of the ciliary body, especially in the depressions between the processes and folds; others lie free on the surface, and in every respect resemble the deposits on the back of the cornea. Groenouw found partial atrophy of the epithelium of the pars plana. The vitreous contained round-cells and fibrillæ, especially in the anterior part, and to some extent in front of the optic disc. The iris was infiltrated and also the deeper layers of the peripheral part of the cornea. Groenouw considers iritis as secondary to the cyclitis. He found the choroid, retina, and optic nerve healthy, but other observers have found them affected (Knies, Fuchs).

Chronic plastic cyclitis is much more commonly met with in the pathological laboratory. Here the exudate is very rich in fibrin and is gradually organised into fibrous tissue. The ultimate result is phthisis bulbi, the picture differing in no respect from the late stages of non-suppurative acute plastic cyclitis. The intermediate stages are best seen in cases of pseudo-glioma, where the difficulty of diagnosis leads to comparatively early enucleation.

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SYMPATHETIC CYCLITIS

The ciliary body in sympathetic ophthalmia usually shows traces of chronic inflammation. The exciting eye may be attacked with the ordinary acute cyclitis as the result of the injury. In other cases it enters into the condition of a subacute or chronic irido-cyclitis. In yet another group of cases the inflammatory symptoms are minimal: there is no keratitis punctata, and only slight irritability, manifested by lacrymation and transient ciliary injection. In one such "dangerous eye" which I have had the opportunity of examining, there were nodules of lymphocytes in the iris and ciliary body—a condition which is not uncommon in chronic inflammation, and may be called *nodular irido-cyclitis* for the sake of distinction. The nodular aggregations are commoner in the iris and choroid than in the ciliary body; they may contain numerous giant-cells, as well as epithelioid cells, so that the resemblance to tubercle is very striking; this occurs more frequently in the choroid than in the ciliary body or iris. The observation of giant-cell systems was first made by Krause (1881), and has since been confirmed by Schirmer, Axenfeld, Pincus, and many others. The giant-cells are often very large, and have many nuclei, which are usually arranged irregularly, but may assume the Langhans type.

The conditions found in the ciliary body of the sympathising eye in the cases which have been examined are, apart from the injury, identical with those in the exciting eye. Sympathetic serous cyclitis has been examined in one case only (Grunert's case, Schirmer); keratitis punctata and infiltration of the whole uveal tract were present. In other cases nodular deposits of lymphocytes, with or without epithelioid and giant-cells, have been observed.

KRAUSE.—A. f. A., x, 1881. SCHIRMER.—A. f. O., xxxviii, 4, 1892. PINCUS.—A. f. O., xl, 4, 1894. AXENFELD.—B. d. o. G., 1897. *SCHIRMER.—In G.-S., 2nd ed., 1900.

SYPHILIS

In syphilis the ciliary body may be diffusely infiltrated with granulation tissue and surrounded by inflammatory exudates. This occurs most commonly when the choroid is probably the primary seat, or is at least most affected; the latter contained giant-cell systems in a case reported by Fialho. The granulation tissue is more frequently localised, and undergoes necrosis, often involving the iris, cornea, and angle of the anterior chamber, as well as breaking through the sclerotic and appearing as an ulcer upon the surface. The latter may have a typical "wash-leather" slough. I have reported three such cases, which were remarkably similar. The following is a description of one of them:

The ciliary body was intensely inflamed and congested, the blood-vessels being dilated and packed with red corpuscles. The ciliary processes were covered with leucocytes, and at the tips the pigment layer of epithelium had become bleached. The origin of the ciliary muscle was intact above. Behind, the whole ciliary body was detached from the sclera, the space being full of a loose pigmented network, which contained albuminous coagulum; the detachment extended back to the equator, posterior to which the choroid was *in situ*. Below, the ciliary body was largely replaced by gummatous infiltration, a few layers of muscle, carrying the very inflamed processes, alone remaining (Fig. 257). All the more external parts had become absorbed; the sclerotic was absorbed here, with the exception of a strand which ran forward to the centre of the mass, where it ended in a necrotic mass. Externally the gumma opened on to the conjunctiva as an ulcer, the episcleral tissues being necrosed. The conjunctiva round the ulcer formed a swollen fold, the epithelium having grown in along the under surface for a considerable distance on each side. The conjunctival stroma consisted of much-dilated vessels surrounded by closely packed round cells. The gumma itself was almost entirely necrotic. It consisted of masses of round-cells with fragments of partially absorbed sclerotic, etc. There were no giant-cells. There were no blood-vessels in the central parts. At the periphery the cells stained better, and showed a zone of inflammatory reaction. On the inner side they were endothelial in type, the smaller round-cells being principally distributed around the vessels. In front round inflammatory cells invaded the cornea, spreading up the spaces between the lamellæ, and separating these widely, so that the cornea was much thickened. A small portion of

the limbus was entirely destroyed, so that the gumma invaded the angle of the anterior chamber. The vitreous was pervaded with leucocytes, mostly aggregated in the lower part. The ciliary processes were pressed inwards, and the softening of the sclerotic had subsequently allowed it to be forced outwards by the subciliary and subchoroidal exudate. The inflammation had travelled outwards in the direction of the lymph- and blood-streams, probably along the course of the anterior ciliary vessels.

Whilst there have been several clinical cases of gumma of the ciliary body recorded, very few have been examined microscopically. The early cases of v. Hippel, Delafield, Barbar, Loring and Eno afford little more than topographical details. Alt records a gumma

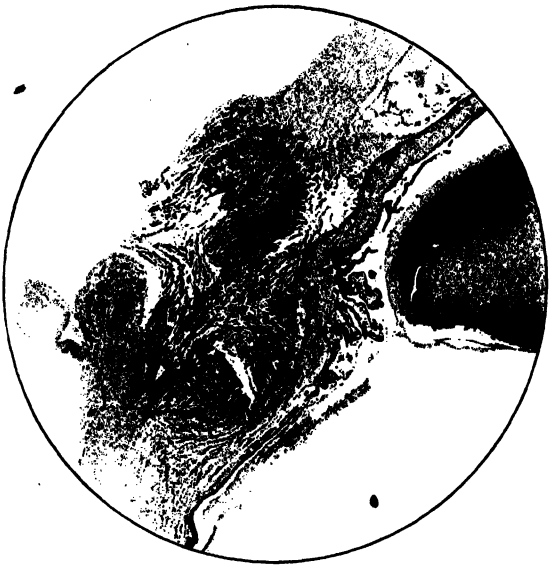


FIG. 257.—GUMMA OF CILIARY BODY. × 8.
Morton and Parsons, T. O. S., xxii.

which was confined to the ciliary body, but does not give many histological details. Scherl's case was much farther advanced, and is remarkable in that the lens was involved. Ostwalt and Coppez give bibliographies of cases recorded up to 1896 and 1898 respectively. The latter describes a case of condyloma of the ciliary body which bears great resemblance to the case recorded above. He lays much stress upon the importance of distinguishing between the earlier secondary and the later tertiary manifestations. It is open to question whether this is possible pathologically, and whether it is of any importance clinically, at any rate in the case of the ciliary body. Coppez carefully analyses previously reported cases according to his views, and supplies useful abstracts of them. Baas reviews the whole subject of syphilis in the eye, and Brixa reports a gumma of the ciliary body, with much loss of tissue and widespread syphilitic changes in other parts of the eye. It

is noteworthy that in most of the cases examined microscopically giant-cells were absent. This accords with Baumgarten's dictum that "in pure gummata giant-cells, especially of the Langhans type, may be entirely absent." He regards their presence as an indication of a mixed infection of syphilis and tubercle. A more recent case is that of Hanke from Professor Fuchs's clinic, and it is remarkably similar to the one recorded above. Fialho, *apropos* of an eye from the same source with very extensive syphilitic lesions showing giant-cells, discusses the accuracy of Baumgarten's conclusions.

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TUBERCLE

Tubercle of the ciliary body is generally an extension of the disease from the iris or choroid. It is not improbable, however, that it commences more frequently in this situation than published records would lead one to suppose, a view which is supported by the susceptibility of the ciliary body to other granulomatous affections. The microscopical characteristics do not differ from those elsewhere in the uveal tract, and do not demand special description. The connective tissue is first involved, the muscle later and in less degree. Large masses are often formed, limited internally by the more or less fragmentary retinal epithelium, externally by the ciliary muscle. Perforation of the globe is especially frequent (Lagrange). Diagnosis rests upon the presence of caseation and the demonstration of tubercle bacilli, either by staining or inoculation.

LEPROSY

The ciliary body is a favourite site for leprosy, which is often primary here as regards the eye. As usual the bacilli are found near the blood-vessels, but less so than in the iris (Lie), in the lymph-spaces around the muscle-fibres, but not in them, and along the nerves. They may also be found in small numbers in the pigment-cells. The muscle-fibres contain the typical lepra pigment granules, staining like the bacilli, but being less acid-fast. The granulation tissue is generally developed only moderately, but may involve and destroy the whole ciliary body (Franke and Delbanco).

(For BIBLIOGRAPHY, *see* "Lids," "Cornea.")

DEGENERATIONS

Senile Degeneration

Senile degenerative changes in the ciliary body are often well marked, and have received minute attention from Kerschbaumer.

The ciliary processes are longer and more branched, and the anterior parts are often swollen, so that the iris is pressed forwards at the periphery; this may be a factor in the causation of glaucoma. They also encroach upon the posterior chamber. The non-pigmented epithelium often shows hyperplasia, the cells proliferating by karyokinesis and forming excrescences (Kuhnt). The cells become convex towards the vitreous, and neighbouring excrescences form a festoon-like arrangement, often with a central lumen; in this manner large cystic spaces may be produced (*v.* p. 358). The pigmented epithelium sometimes participates in the proliferation (Kuhnt, Kerschbaumer).

The basal hyaline membrane increases in thickness from the age of forty onwards. The outer part loses its hyaline character and becomes granular. The fibres of the inner network become thickened.

The connective tissue is thickened throughout, and often becomes hyaline. The vessels show signs of sclerosis, the walls becoming thick, fibrillated, or hyaline, and the lumina contracted.

The muscle fibres degenerate, many nuclei disappearing and the bundles becoming thin. The intermuscular spaces contain hypertrophied connective tissue, fluid, or granular coagula.

Kuhnt.—K. M. f. A., xix, 1881. Kerschbaumer.—A. f. O., xxxiv, 4, 1888.

Atrophy

Atrophic changes in the ciliary body are common after cyclitis and in old glaucomatous eyes. When moderately pronounced, there is marked connective-tissue hyperplasia, with atrophy of the higher tissues. The ciliary body is pervaded with thick bands of fibrillar or hyaline connective tissue, the muscle bundles are thin, and have lost many of their nuclei, though complete atrophy is rare (Figs. 255, 258). The blood-vessels are sclerosed. The ciliary processes are thin, shrunken, and reduced in number, though some are often drawn out into the vitreous and are longer than normal. The whole ciliary body is flattened and much reduced in size.

These changes are accompanied by a diminished secretory activity, so that a previously increased intra-ocular tension may be reduced far below normal.

Calcification and Ossification

Calcification and ossification of the ciliary body itself is rare, and is nearly always a sequel of ossification in the choroid. The process is

similar, and will receive detailed description in treating of the choroid. The same changes more frequently occur in cyclitic membranes and deposits, and have been described elsewhere (*v.* p. 346).

CYSTS

Kuhnt (1881) first described cysts of the ciliary body as a senile change. They occur principally in the pars plana, near the ora serrata, and are formed by separation of the non-pigmented from the pigmented layer of cells. They are therefore similar to those cysts of the iris which are caused by separation of the two layers of pigmented retinal epithelium. Others are formed by separation of the pigment layer from the underlying ciliary body. Larger cysts arise by confluence of smaller ones. The phenomenon is due to abnormalities in the transudation of lymph, and is always the result of degenerative, and often of inflammatory, conditions. This is shown by the atrophic condition of the ciliary body in the cases.

Cystic spaces produced by "detachment of the pars ciliaris retinæ from the subjacent pigment layer" were also noticed by Brailey (1882). When associated with cyclitis they contained corpuscular elements.

The largest cysts of the ciliary body were described by Greeff, and resulted from atrophy of the ciliary body after irido-cyclitis following cataract extraction for a traumatic cataract. The eye was removed seven years after the operation, and was in a condition of phthisis bulbi with complete detachment of the retina. The cysts were observed ophthalmoscopically. Behind the cornea were two cysts, the outer 7·5 mm. broad and 6·5 mm. high, the inner 5 mm. broad and 8 mm. high. The thin walls were pigmented and enclosed a clear fluid. The ciliary body was completely atrophic, the processes being pressed aside and appearing as dark pigmented bands. The epithelium of the pars ciliaris retinæ was no longer recognisable. The cyst-wall was lined by a single layer of flattened "endothelial" cells; the atrophic pigmented uveal tissue formed the outer part of the wall.

Greeff explains these cysts on the theory of retained secretion of Treacher Collins's glands. After the extraction of the traumatic cataract a slow irido-cyclitis led to adhesion of some of the ciliary processes to each other and to the ciliary body. Closed spaces were thus formed, into which more and more serous fluid was poured. As the cysts grew the cylindrical epithelium became flattened, so that a single layer of flattened cells resulted.

Treacher Collins mentions an eye with cyclitis which showed cysts due to the distension of the glands. He states that such cysts "would differ from those due to detachment of the pars ciliaris retinæ from the pigment epithelium in being bounded entirely by pigment-cells."

KUHNT.—K. M. f. A., xix, 1881. BRAILEY.—R. L. O. H. Rep., x, 1882. HERSCHBAUMER—A. f. O., xxxiv, 4, 1888. GREEFF.—A. f. A., xxv, 1892. TREACHER COLLINS.—Researches, London, 1896.

TUMOURS

Epithelial Hyperplasia

We have seen that epithelial hyperplasia occurs in old age (Kuhnt, Kerschbaumer), with the formation of small festoon-like thickenings, and also in cyclitis (Alt, Treacher Collins), with the formation of non-pigmented and pigmented bands and tubes or tumour-like thickenings. Krückmann describes small nodules of granulation tissue covered by epithelium, which sprout out into the vitreous in cyclitic conditions.



Fig. 258.—Epithelial Hyperplasia of Ciliary Body. × 55.
Note the fibrous degeneration of the ciliary body itself. (R. L. O. H. Rep., xv.)

The granulation tissue shrinks later, so that spaces covered with epithelium are formed in the scar tissue. Only rarely does the epithelium appear to invade the preformed tissues, and these are then found to be in a sclerosed cicatricial condition.

Hanke described an "epithelioma" of the ciliary processes in a woman æt. 65. The new growth commenced under the epithelium, was reniform in shape, with the hilum directed towards the vitreous. The two layers of retinal epithelium were continued over the tumour, the outer layer being less pigmented over the convexity. This layer remained one cell thick, whilst the inner, non-pigmented layer formed a network of bands and nests with spaces between them.

Some of Alt's cases (*v.* p. 360) undoubtedly belong to the same category.

I have met with a growth in every respect resembling Hanke's, occurring in a man æt. 65. On one ciliary process below was a globular mass on the anterior surface, with its long axis in the direction of the process. It was about 1 mm. long by 0·75 mm. wide. The non-pigmented retinal epithelium could be traced on to its surface, whilst the pigmented epithelium was continued under it, though the cells soon lost their pigment, which was also absent or scanty on many of the processes. The main mass of the swelling consisted of irregular groups of cells resembling the non-pigmented epithelium, lying in a hyaline matrix, with numerous irregular spaces. The nuclei stained faintly, were round or oval; the outlines of the cells were indistinct. No tubular arrangement of the cells could be demonstrated, though the general disposition was suggestive of such an arrangement.

It is clear, I think, that these cells are due to the proliferation of the non-pigmented or inner layer of the retinal epithelium, and that the proliferation has taken place into the vitreous body, the underlying ciliary process showing the same condition as the others. There was no evidence of inflammation, such as infiltration with leucocytes, either in or around the mass.

Schlipp reported an epithelial tumour of the ciliary body in the shrunken globe of a girl æt. 10. The posterior part of the globe was almost filled with pigmented and non-pigmented epithelium, often arranged in bands. The cells were large and polygonal; many of the nuclei were much swollen, and the cytoplasm contained fatty and hyaline globules. There were no giant-cells or caseation. The bands were separated by connective tissue with scant blood-supply and bone.

KRÜCKMANN.—IX Internat. Ophth. Congress, Utrecht, 1899. HANKE.—A. f. O., xlvii, 1899. PARSONS.—R. L. O. H. Rep., xv, 4, 1903. SCHLIPP.—A. f. O., xlviii, 1899.

ADENOMA

Several epithelial growths have been described as *adenomata*. Fuchs described a nodule with adenoma-like structure between two folds of a ciliary process in a case of chronic uveitis with glaucoma. It occurred in a woman æt. 70. The cellular bands lay embedded in a homogeneous mass, and the nodule received a blood-vessel from the ciliary body, the walls of which were pigmented. It was probably a simple epithelial hyperplasia (*v.* p. 359).

Pergens described an adenoma 0·75 mm. long by 0·25 mm. broad in the ciliary body of a man æt. 56. The eye had been injured by a piece of iron four years before, and had had two iridectomies. The growth consisted of tubules of epithelium lying in a gelatinous material.

Alt has reported five cases of adenoma of the ciliary body, mostly in the eyes of old people. The growths were generally microscopic in size, and were in all cases found incidentally in the course of routine examination. Two eyes were removed *post mortem* from a case of croupous pneumonia; the third was enucleated for sarcoma of the conjunctiva; the fourth was a traumatic suppurative panophthalmitis; the fifth was

removed on account of an injury. Most of these belong to the type of epithelial hyperplasias.

In the typical cases the non-pigmented epithelium bursts through the pigmented layer, and grows in bands and tubules in an amorphous or gelatinous matrix; the cells often show colloid degeneration. The surrounding tissues appear to be passive, and show no reaction.

The published cases of adenoma are too few and too anomalous to permit of dogmatic statements. The diagnosis of an adenoma presupposes the existence of glands, and this question must still be regarded as *sub judice*. On the other hand, looked at from the point of view of inflammatory or degenerative hyperplasia (Emmanuel, Krückmann), there is no such theoretical foundation, whilst it must at the same time be admitted that simple hyperplasia does not usually assume such an atypical complexity of structure.

FUCHS.—A. f. O., xxix, 4, 1883. PERGENS.—A. f. A., xxxii, 1896. ALT.—Amer. Jl. of Ophth., xv, 1898. TREACHER COLLINS.—Researches, London, 1896. EMMANUEL.—Virchow's Arch., clxi, 1900. KRÜCKMANN.—IX Internat. Congress, Utrecht, 1899.

CARCINOMA

Primary carcinomata of the ciliary body have been described by v. Michel, Treacher Collins, and Badal and Lagrange.

v. Michel (1878) described an "endothelial and epithelial cancer of



FIG. 259.—MELANOTIC CARCINOMA (?) OF CILIARY BODY. × 300.
From Treacher Collins. Bleached section. (T. O. S., xi.)

the ciliary body." He has since arrived at the conclusion that it was a pure endothelial growth (Emmanuel) (*v.* p. 363).

Treacher Collins (1891) described an epithelial growth in a girl of

nineteen, and another in a woman of sixty-three, who twenty-seven years previously had had a severe blow on the eye from a fist, and two years after had found that it was blind. The growth was partially pigmented, sprang from the ciliary processes, and invaded the ciliary muscle and root of the iris. It had epithelial tubules, and had partially undergone colloid degeneration (Fig. 259). It was regarded as a primary melanotic glandular carcinoma.

Badal and Lagrange (1892) described a primary carcinoma of the ciliary body in a boy æt. 8. The eye had been blind three years, and had an intercalary staphyloma. There were two white nodules close together in the ciliary region, and these were composed of (1) regular tubules with a central lumen, lined by a single layer of cylindrical epithelium; (2) similar tubules filled with proliferating epithelial cells;



FIG. 260.—CARCINOMA OF CILIARY BODY. × 300.
Snell and Treacher Collins, T. O. S., xix.

(3) collections of atypical and deformed epithelial cells grouped and separated by thin strands of connective tissue.

Treacher Collins (1893) described another tumour of the ciliary body with glandular structure, in a woman æt. 28. Vision had been failing for six months. The anterior part of the tumour was deeply pigmented, the posterior part devoid of pigment. Microscopically the cells composing the central portions of the growth appeared very degenerate; they were much swollen and their outlines were ill defined. The more peripheral parts were less degenerated; the cells here were of epithelial character, and arranged in a way suggestive of a glandular structure.

The very extensive carcinoma-like intra-ocular growth reported by Snell and described by Treacher Collins resembles those already mentioned (Fig. 260), but its site of origin is impossible to determine.

The same criticisms relative to adenomata apply with equal force to the primary carcinomata of the ciliary body.

Secondary carcinoma of the ciliary body is usually by continuity from the choroid, and is very rare. Two cases are on record (Ewing, Abelsdorff); in each case metastatic carcinoma of the choroid followed a primary growth in the breast. In both cases the ciliary muscle fibres were pushed apart by nests of epithelial cells. The ciliary processes, especially the anterior ones (Abelsdorff), were also involved, but only to a small extent. In Abelsdorff's case the root of the iris was also invaded.

Treacher Collins.—T. O. S., xi, 1891; xiv, 1894.; Researches, London, 1896. Badal and Lagrange.—A. d'O., xii, 1892; Lagrange.—Tumeurs de l'Œil, i, Paris, 1901. Ewing.—A. f. O., xxxvi, 1, 1890. Abelsdorff.—A. f. A., xxxiii, 1896. Snell.—T. O. S., xix, 1899.

Glioma

Emmanuel described a case of **primary glioma** of the ciliary body. The patient was a child æt. 5½. The pupil had been elongated downwards since birth; there was a large ciliary staphyloma around the cornea. In the staphyloma was a growth 10 mm. long by 6 mm. broad. The tumour started in the pars ciliaris retinæ, and consisted of bands of cells arranged in folds and networks; rosettes were also present in large numbers. Emmanuel regards Badal and Lagrange's case as a glioma. The term neuro-epithelioma is perhaps the least objectionable name for such neoplasms. In any case they must not be regarded as gliomata in the sense of being derived from or containing neuroglia.

Hirschberg and Happe reported a case of glioma endophytum starting in the pars ciliaris retinæ and the immediate neighbourhood.

Helfreich described a gliomatous proliferation in a microphthalmic eye, containing folded bands, which sprang from the ciliary processes.

Secondary glioma usually attacks the ciliary body from the choroid, but may also do so from the supra-choroidal space or from the inner surface. In late stages the ciliary body is replaced by the growth, its contour only being marked out by a line of pigment; the ciliary processes succumb last, and finally no trace of the ciliary body is left (Wintersteiner).

Emmanuel.—Virchow's Archiv, clxi, 1900. Hirschberg and Happe.—A. f. O., xvi, 1, 1870. Helfreich.—A. f. O., xxi, 2, 1875. Wintersteiner.—Das Neuroëpithelioma Retinæ, Leipzig and Wien, 1897.

Endothelioma

The tumour first described by v. Michel (1878) as an "endothelial and epithelial cancer of the ciliary body" has since been regarded by the author as of pure endothelial origin (Emmanuel). It occurred in a woman, æt. 41, who had always had good health; the eye was removed for supposed sarcoma of the iris and ciliary body. The tumour con-

sisted of a fine network of connective tissue, carrying a few vessels. Cylindrical cells were arranged like a pallisade upon both sides of the connective tissue, and bounded narrow spaces. Hence the appearance of a tubular gland was simulated. Elsewhere there were large multinucleated cells with branching processes; these might well have originated in endothelial cells, but could scarcely be derived from cylindrical epithelium. The tumour showed some slight tendency to invade the normal tissues, but grew mostly towards the vitreous.

Another endothelioma of the ciliary body, partially pigmented, has been described by Schleich (1880). Large, closely packed, non-pigmented, polygonal cells surrounded capillary vessels, which possessed no definite walls of their own, and which were derived from the ciliary vessels. Between the epithelioid cells were large round cells filled with dark granules of uveal pigment, and a smaller number of small branching and spindle-shaped cells with lighter pigment, resembling the normal chromatophores. At a fairly uniform distance from the vessels were spaces filled with hyaline material. Schleich regarded the tumour as derived from endothelial cells at the anterior part of the ciliary body, near the angle of the anterior chamber. From the description, the growth might be looked upon as a peritheliôma.

Emmanuel regarded Groenouw's case of "unpigmented alveolar flat sarcoma" of the ciliary body as a case of endothelioma (*v.* p. 372).

It will be seen that it is impossible to arrive at any definite conclusion as to the true nature of these rare growths. The name under which they are described is often the offspring of the author's preconceived ideas; and in most cases the actual description bears obvious traces of the same unconscious influence.

v. MICHEL.—A. f. O., xxiv, 1, 1878. SCHLEICH.—Mittheilungen aus der ophth. Klinik zu Tübingen, i, 1880.

MYOMA, MYOSARCOMA

A small number of tumours of the ciliary body have been described as myomata or myosarcomata. The difficulties of substantiating this diagnosis are very great, and are considered by Mitvalski to be insuperable. The presence of unstriped muscle-fibres normally in this situation may easily lead to confusion in the early stages of a new growth. Moreover, young muscle cells have not such a characteristic rod-shaped nucleus as the adult cell, but resemble much more nearly the branching embryonic connective-tissue cells which are found in spindle-celled sarcomata. *Per contra*, large sarcomatous spindle cells may have rod-shaped nuclei, rounded at the ends, and often somewhat bent, exactly like muscle cells. No trustworthy differential stain has yet been found, though there are indications that such a stain will probably be devised.

Myomata have been described by Iwanoff (1867), Solomon (1882), Mules (1888), Deutschmann (1890), Lange (1890), and Lagrange. In all cases there has been doubt as to the diagnosis, which has lain between myoma and spindle-celled sarcoma, and in most cases those

who have seen the actual preparations have failed to agree. Under these circumstances it seems best to refer readers to the original communications for further details.

IWANOFF.—In G.-S., iv, pp. 6 and 8, 1876. SOLOMON.—T. O. S., ii, 1882. MULES.—T. O. S., viii, 1888. DEUTSCHMANN.—B. z. A., i, 1890. LANGE.—A. f. O., xxxvi, 3, 1890. LAGRANGE.—Tumeurs de l'Œil, i, Paris, 1901. MITVALSKI.—A. f. A., xxviii, 1894.

SARCOMA

Primary sarcoma of the ciliary body is a rare disease, though the fifty or sixty recorded cases give little idea of its relative frequency. It often manifests itself first by localised injection or pigmentation of the

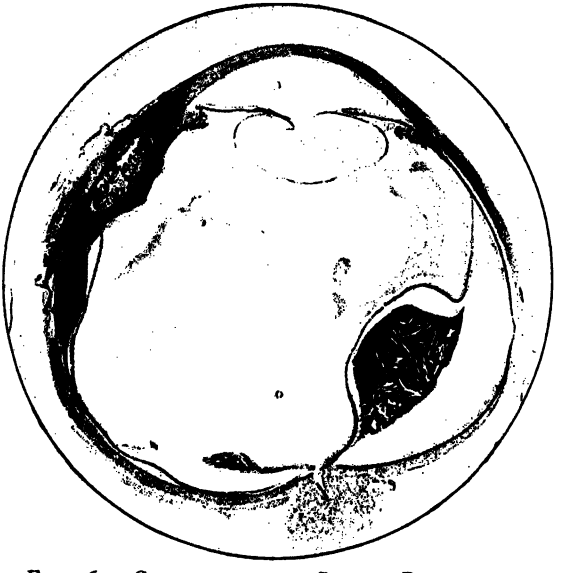


FIG. 261.—SARCOMA OF THE CILIARY BODY. × 3.

From a woman æt. 50. Horizontal section. Melanotic spindle-celled sarcoma of ciliary body on outer side, with large central degenerated area. Simple detachment of retina on inner side. The growth is commencing to invade the a. c., and has already extended along the anterior perforating vessels, forming several episcleral nodules.

ciliary region, or by growing forward into the anterior chamber. In the latter event it usually pushes the iris away from its peripheral attachment, and produces an irido-dialysis (Fig. 262). The cause of this symptom may be recognised by the pigmentation of the growth, or by the observation of vessels upon its surface. The course of the disease runs through the four stages characteristic of all intra-ocular growths, viz. (1) localised growth: this differs from choroidal sarcoma in that detachment of the retina does not occur, or occurs late, owing to the firmer union of the pars ciliaris retinæ and the region of the ora serrata to the underlying uveal tract; (2) increased tension: this is said

to occur later in ciliary sarcoma than in that of the choroid (Devereux Marshall); (3) extra-ocular extension: this occurs relatively early, owing to the proximity of the anterior perforating vessels, and to the prevalent direction of the lymph-stream outwards; (4) general metastasis: this differs in no respect from that of choroidal sarcoma.

It is often impossible, both clinically and pathologically, to distinguish between peripheral choroidal and primary ciliary sarcomata.

Fuchs (1882) found 22 cases of sarcoma of the ciliary body amongst 259 of the uveal tract (9 per cent.); of these 2 were non-pigmented. In situation, 6 were out, 4 in, 2 up, 4 down, 6 unknown. Out of 8 cases in which the point could be determined, 4 arose from the outer layers, 2 from these or from the ligamentum pectinatum, 1 from the

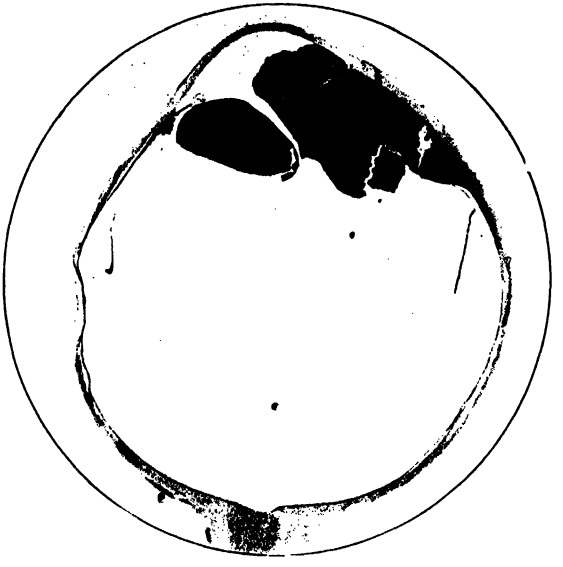


FIG. 262.—SARCOMA OF CILIARY BODY INVADING ANTERIOR CHAMBER. × 3.

From a man æt. 68. Melanotic spindle-celled sarcoma of ciliary body, growing forwards into the anterior chamber. Note the subluxation of the lens.

ciliary muscle, and 1 from the ciliary processes; 6 were round-celled, 7 spindle-celled, 3 mixed round- and spindle-celled; 1 was a myosarcoma, 1 an endothelial sarcoma, and 4 were unknown.

Mules (1888) collected 27 cases, details of which are tabulated in his article.

Lawford and Treacher Collins (1890) found 6 cases in 103 cases of sarcoma of the uveal tract examined at Moorfields: all were pigmented; 2 were spindle-celled, 1 large polygonal-celled, 3 mixed round- and spindle-celled.

Kerschbaumer (1900) found 8 cases in 67 of sarcoma of the uveal tract, chiefly from the Leipzig clinic. Of these most were spindle-celled; these were of relatively slow growth, showing fewer mitoses and

multinucleated cells, and appeared to be relatively benign; 3 were pigmented, 3 were leuco-sarcomata with hæmatogenous pigmentation, and 2 were pure leuco-sarcomata.

Groenouw (1898) collected 50 cases from the literature, including the so-called myomata and myosarcomata. Of these, 5 were leuco-sarcomata, 45 were melanotic; this agrees fairly with Fuchs's results for the whole uveal tract, in which 12 per cent. were non-pigmented. Lawford and Collins found 6 per cent. non-pigmented for the whole uveal tract, so that a comparison of this result with that of Groenouw for the ciliary body only (10 per cent.) supports Fuchs's view that leuco-sarcomata are commoner in the anterior portion of the uveal tract than in the posterior. The inclusion of the myosarcomata and of an endothelioma (alveolar sarcoma) must be borne in mind.

Of 30 cases, Groenouw found 7 round-celled, 13 spindle-celled, and 10 mixed-celled; this is opposed to Fuchs's rule that round-celled sarcomata are commoner in the anterior, spindle- and mixed-celled in the posterior part of the eye.

The average age for the round-celled type was 35, for the spindle-celled and for the mixed-celled 44, as opposed to 38, 45, and 49 for the whole tract (Fuchs). The average duration of the growths at the time of operation was $7\frac{1}{3}$, $13\frac{1}{2}$, and $11\frac{1}{2}$ months respectively, as opposed to $18\frac{1}{2}$, 30, and 34 months for the whole tract (Fuchs). This shows that ciliary sarcomata are operated upon at an earlier stage; it further agrees with Kerschbaumer's later result for a different set of cases that round-celled are more rapid in growth than spindle-celled.

The average age of patients with leuco-sarcomata of the ciliary body was 32 (10 to 48), with melanotic 44 (10 to 74), as compared with 30 and 46 respectively for the whole tract (Fuchs). Out of 5 non-pigmented and out of 44 pigmented 1 was ten years old in each case; as far as percentages are of any value at all for such small numbers, this agrees with Fuchs's estimates for the whole tract, viz. 20 per cent. and $1\frac{1}{3}$ per cent. respectively.

The occurrence in consecutive decades was as follows:

Age.	Ciliary body.	Uveal tract (Fuchs)
1—10 ...	2 ...	11
11—20 ...	5 ...	16
21—30 ...	5 ...	19
31—40 ...	9 ...	43
41—50 ...	11 ...	55
51—60 ...	7 ...	55
61—70 ...	8 ...	25
71—80 ...	2 ...	10
	49	234

As regards sex, 21 men and 29 women had ciliary sarcomata, 137 men and 116 women sarcomata of the uveal tract (Fuchs).

The side affected was—right, 23 ciliary body and 108 uveal tract; left, 24 and 101; both, 1 and 5.

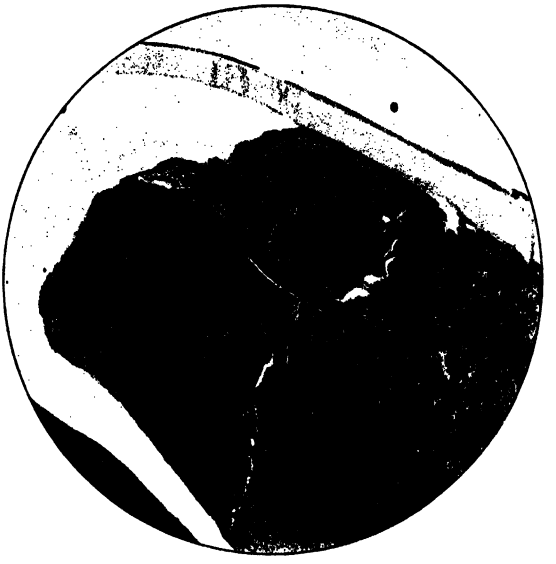


FIG. 263.—SARCOMA OF CILIARY BODY INVADING ANTERIOR CHAMBER. × 10.

From the same specimen as Fig. 262. The iris is seen embedded in the growth; the pupillary edge with the sphincter iridis is seen at the anterior part. The lens has been pushed aside.

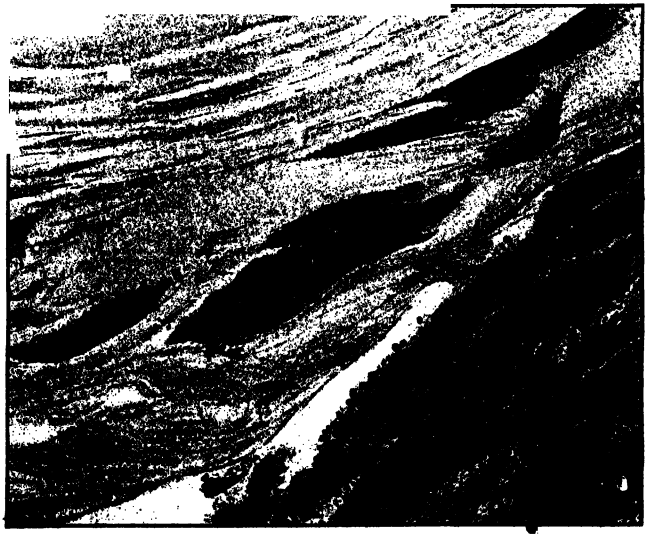


FIG. 264.—SARCOMA OF CILIARY BODY INVADING LENS. × 60.

After Lawford, R. L. O. H. Rep., xi. Showing invasion of the posterior part of the lens by a melanotic sarcoma of the choroid and ciliary body.

The prognosis is equally unfavourable for each group of cases. Seventeen cases treated by enucleation were followed for 1 year or more; local recurrence occurred in 2, 1 of which died, and the other was described as a myoma, and the recurrence took place after 5 years. Metastases occurred in 4 cases, twice in the liver, once in the stomach or liver and in the skin, once apparently in the other eye, ending in death at the end of a year. Eleven were healthy—2 cases after 1 year, 3 after 1–2 years, 3 after 2—3 years, 1 after 3½ years, 2 after 5 years (Groenouw).

Sarcoma of the ciliary body grows almost exactly like that of the choroid, but the anatomical relations of the part lead to slight differences. It usually forms a rounded projection into the vitreous, the thickness of which is rather less than the length. It does not so frequently assume the mushroom shape, with head, neck, and base, which is so characteristic of the choroidal growth, and this is partly due to the splitting up of Bruch's membrane. When the tumour starts in the anterior part of the ciliary body, and in the later stages of one starting farther back, it invades the posterior chamber, pushing aside the lens and pushing forward the iris. The iris is directly invaded by continuity, and may become embedded in the growth (Fig. 263). It is often pushed inwards, so that the growth appears in the angle of the anterior chamber and gives rise to irido-dialysis, as already mentioned. It may then progress until it fills the anterior chamber.

The lens is at first merely pushed aside or distorted, but its nutrition is later interfered with, so that it becomes opaque. This opacity may assume the form of a posterior cortical cataract (Becker, Salzmann). The capsule, like all hyaline membranes, offers great resistance to invasion, and is very rarely broken through. It was ruptured in Lange's case ("myosarcoma"). Involvement of the lens in the growth is of extreme rarity. Such an event has, however, been recorded by Lawford (Fig. 264). Small islands of sarcoma-cells lay in the lens substance between the lamellæ over a very restricted area. They appeared to have effected an entrance a little distance behind the equator, *i.e.* where the capsule is naturally much thinner and less resistant than anterior to the equator. Continuity between the islands in the lens and the main growth in the ciliary body could not be traced.

In many cases the lens is merely subluxated, but distortion may be extreme. It may be simply flattened or more or less deeply excavated. In Webster and Schwarzchild's case it was triangular in section.

Detachment of the retina occurs only in the later stages, and is naturally posterior to the growth. It was absent in most of the cases examined.

Epibulbar extension takes place along the perforating anterior ciliary vessels, especially the veins (Fuchs), and is of frequent and comparatively early occurrence. There is usually direct continuity of the cells along the perivascular lymph-spaces, but the most exhaustive investigation may fail to trace any continuity (Groenouw). In this case the cells are probably carried by the lymph-stream, and it is interesting in this connection to note that in Groenouw's case the

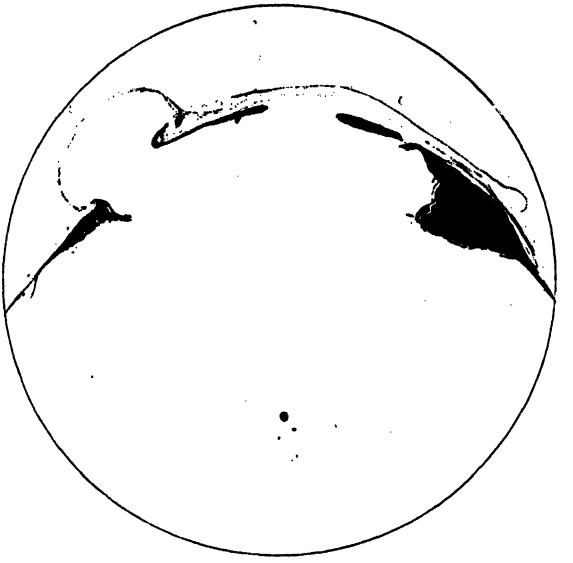


FIG. 265.—ANNULAR SARCOMA OF CILIARY BODY. × 4.

From a boy æt. 14 (*see* Text, and A. f. O., lv, 2, 1903). Note the infiltration of the iris; also the intercalary staphyloma.

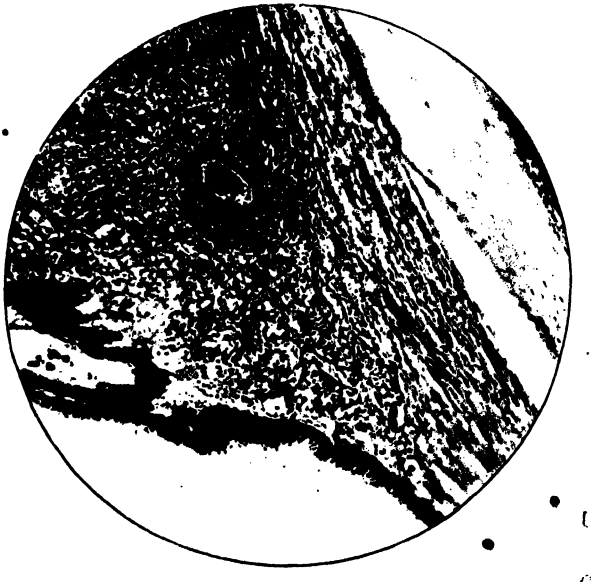


FIG. 266.—ANNULAR SARCOMA OF THE CILIARY BODY. × 65.

From the same specimen as Fig. 265. The ciliary muscle is seen to the right, the cells being quite different from those of the growth.

growth was an alveolar sarcoma, *i. e.* probably an endothelioma. In nearly all cases with epibulbar extension of the growth there is increased intra-ocular tension (Fuchs). It is not always easy to determine whether the epibulbar tumour is secondary to the intra-bulbar one, or *vice versâ*. This is shown, for example, in the case reported by Verhoeff and Loring. The tension of the eye may afford valuable evidence in settling this point, and it must further be remembered that intra-ocular extension of extra-bulbar growths is comparatively rare, and occurs at a late stage.

The minute histology of sarcoma of the ciliary body—the nature and arrangement of the cells, pigmentation, blood-vessels, etc.—is



FIG 267.—IRIS FROM CASE OF ANNULAR SARCOMA OF CILIARY BODY. × 65.

From the same case as Figs. 265, 266. The iris is little changed in form, but it is densely infiltrated with tumour cells. The pupil is to the left. Note the very wide "ectropion of uvea."

identical with that of sarcoma of the choroid, and will be fully discussed in that connection.

Devereux Marshall has described a rare case in which the growth was mainly composed of a large cyst, whilst the more solid part also contained numerous cystic spaces of variable size. It was a mixed round- and spindle-celled melanotic sarcoma.

It is extremely rare for sarcoma of the ciliary body to be multiple, but a case of two small spindle-celled sarcomata on opposite sides of the eye has been recorded by Taylor.

A rare form of sarcoma of the ciliary body is distinguished by its flatness and infiltrating character, so that it extends widely with little true tumour formation. Owing to this it generally invades the whole

circle of the ciliary body, and may therefore be termed a *ring sarcoma* (Ewetzky) or *annular sarcoma*. It shows the same features as the rare flat sarcoma (Flächensarkom) of the choroid (q. v.).

I have described an annular sarcoma of the ciliary body which was found in the eye of a boy æt. 14. The eye had been injured by a kick seven years previously, and was removed on account of a ciliary staphyloma. The ciliary body below was the seat of a leuco-sarcoma (Fig. 265). Only a small part of the ciliary muscle was intact; this constituted the posterior part, and it was sharply delimited from the new growth (Fig. 266). Traces of the ciliary processes were seen upon the surface, but they were mostly flattened out, the growth being covered by the two layers of retinal epithelium, which were little altered. The growth was a typical spindle-celled sarcoma; the individual cells were of medium length, and had large oval nuclei. There was no difficulty in distinguishing them from the neighbouring unstriped muscle-cells. The growth was very vascular. There were a few small patches of dense pigment, mostly near the surface. These had every appearance of being retinal epithelium, and were portions of the superficial pigmented epithelium of the ciliary processes which had been enclosed in the growth. They were not in intimate relation with the blood-vessels; the spindle-cells and the intercellular substance, where visible, were quite free from pigment.

The growth was of the infiltrating type. It was about 2 mm. in thickness at the thickest part, below. It had, however, infiltrated the whole ring of the ciliary body, the upper part being entirely replaced by sarcoma cells. The iris stroma was similarly replaced below and much infiltrated above (Fig. 267). The cornea and sclera at the limbus below were also infiltrated, the cells growing along the planes of these tissues in their inner layers. The iris above consisted of a small knob, in which traces of the sphincter could be seen. It had a cap of sarcoma cells; peripherally it was firmly adherent to the cornea, was largely replaced by sarcoma cells, and had a dense layer of retinal pigment behind. Below, the iris was free for 2 mm.; it was thickened, but retained its normal shape. The stroma was entirely replaced by new growth. It was covered behind by dense retinal pigment, which extended over the edge and along the anterior surface to about $\frac{1}{2}$ mm. from the attachment to the cornea.

The staphyloma consisted of a very thin layer of fibrous tissue, the deeper layers of which contained many nuclei; it was apparently free from sarcoma cells.

Ewetzky's case 8 was a typical and, up to that time (1898), unique annular sarcoma. It was limited to the iris and ciliary body, and extended around the whole circumference. It very nearly resembled the case described above, except that the tumour was slightly pigmented.

Groenouw recorded in detail the case of a man æt. 28, who received a blow upon the left eye; three weeks later a swelling was noticed at the lower edge of the cornea, and six weeks after this there was a smaller one up and in. After enucleation the eye was found to be enlarged in all dimensions; the growth infiltrated the ciliary body for more than

half the circumference at the lower and inner part. No communication could be found between the ciliary and the epibulbar growths. The ciliary growth was alveolar, non-pigmented, with polygonal, round, and fusiform cells, showing myxomatous degeneration in parts. In places the cells were epithelioid in type. The retina was *in situ*, covered internally and infiltrated with endothelial cells. The disc was cupped. The ciliary growth was infiltrating, distorting the parts but little.

Another typical ring sarcoma has been published, viz. that by Kopetzky von Rechtperg; this one was deeply pigmented. There is every reason to suppose that it had existed for at least twelve years, and slow growth is indeed apparently characteristic of all these infiltrating sarcomata.

Meyerhof described the case of a man, æt. 72 (case iv), with an unpigmented "Flächensarkom" which, starting in the ciliary body, spread forwards into the iris and backwards into the choroid. Two narrow prolongations passed round the root of the iris for several millimetres, but did not meet upon the opposite side. Meyerhof also recorded another incomplete one which was pigmented. This occurred in a woman æt. 60. It invaded both choroid and iris, and there was a small metastasis in the pupillary edge of the iris. The base of the iris and angle of the anterior chamber were densely infiltrated almost completely round the eye, forming two narrow tongue-shaped prolongations running circumferentially above and below the cornea. Spindle-shaped cells could also be seen in the area between these, so that the growth was really completely annular. Meyerhof also recorded (case vi) another pigmented complete ring sarcoma, which formed a circumscribed tumour where it started in the ciliary body.

There are, therefore, now six cases of annular sarcoma of the ciliary body on record.

Secondary sarcoma of the ciliary body is invariably by continuity from the choroid or iris. (*See also* "Sarcoma of the Choroid").

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